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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	FEB 25	CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS	4	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	5	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	6	FEB 28	MEDLINE/LMEDLINE reloaded
NEWS	7	MAR 02	GBFULL: New full-text patent database on STN
NEWS	8	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS	9	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	10	MAR 22	KOREAPAT now updated monthly; patent information enhanced
NEWS	11	MAR 22	Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS	12	MAR 22	PATDPASPC - New patent database available
NEWS	13	MAR 22	REGISTRY/ZREGISTRY enhanced with experimental property tags
NEWS	14	APR 04	EPFULL enhanced with additional patent information and new fields
NEWS	15	APR 04	EMBASE - Database reloaded and enhanced
NEWS	16	APR 18	New CAS Information Use Policies available online
NEWS	17	APR 25	Patent searching, including current-awareness alerts (SDIs), based on application date in CA/CAplus and USPATFULL/USPAT2 may be affected by a change in filing date for U.S. applications.

NEWS EXPRESS	JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005
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NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 16:42:20 ON 26 APR 2005

=> FIL STNGUIDE
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 22, 2005 (20050422/UP).

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=> file hcaplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.06	0.27

FILE 'HCAPLUS' ENTERED AT 16:42:37 ON 26 APR 2005
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FILE COVERS 1907 - 26 Apr 2005 VOL 142 ISS 18
FILE LAST UPDATED: 25 Apr 2005 (20050425/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s testosterone
L1 57193 TESTOSTERONE

=> s l1 and prodrug
9747 PRODRUG
L2 48 L1 AND PRODRUG

```
=> s l2 and ether
        459975 ETHER
L3           6 L2 AND ETHER

=> s l2 and ester
        560072 ESTER
L4          17 L2 AND ESTER

=> d l3 1-6 ibib hitstr abs

L3   ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2002:977668  HCAPLUS
DOCUMENT NUMBER:          138:61309
TITLE:                    Enhanced steroidal drug delivery in transdermal
                          systems
INVENTOR(S):              Houze, David; Nguyen, Viet
PATENT ASSIGNEE(S):       Noven Pharmaceuticals, Inc., USA
SOURCE:                   PCT Int. Appl., 49 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2002102390         A1    20021227    WO 2002-US16579         20020618
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     EP 1406633            A1    20040414    EP 2002-749537          20020618
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     BR 2002010516         A     20041005    BR 2002-10516           20020618
     JP 2005500299         T2    20050106    JP 2003-504976          20020618
     US 2003152613         A1    20030814    US 2002-330279          20021230
     US 2003152614         A1    20030814    US 2002-330360          20021230
     US 2003152615         A1    20030814    US 2002-330361          20021230
     US 2003232073         A1    20031218    US 2002-330281          20021230
PRIORITY APPLN. INFO.:                        US 2001-298381P     P   20010618
                                              US 2001-948107      A   20010907
                                              WO 2002-US16579     W   20020618
AB   A composition for transdermal administration resulting from an admixt. includes
     a therapeutically effective amount of a drug that includes a parent drug and
     a prodrug and a carrier, wherein the parent drug and
     prodrug are individually present in an amount sufficient for a
     pharmacol. effect.  The admixt. include: a therapeutically effective amount
     of a steroid and a steroid derivative and a carrier for the steroid.  The
     steroid and the corresponding derivative are present in a weight ratio of 10:1
to
     1:10 steroid-corresponding steroid derivative  In a preferred embodiment ratio
     is 6:1 to 1:6.  In a preferred embodiment, the corresponding steroid
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derivative is a steroidal ester. In another preferred embodiment, the carrier is a polymer that includes a pressure-sensitive adhesive. In another preferred embodiment, the parent drug is an ACE inhibitor such as ramipril and the **prodrug** is an ACE inhibitor **prodrug** such as ramipril Et and/or Me esters. Thus, a transdermal delivery system contained norethindrone 1.2, estradiol 0.9, norethindrone acetate 2.5, VA-64 15.0, GMS-737 (acrylic PSA), oleic acid 3.0, dipropylene glycol 9.0, and Bio-PSA-7-4603 63.4%.

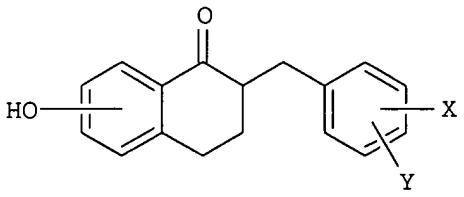
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:435015 HCAPLUS
DOCUMENT NUMBER: 135:33380
TITLE: Benzyl tetralins, formulations and uses thereof as inhibitors of 17β-hydroxy steroid dehydrogenase for treatment of androgen- and estrogen-mediated diseases
INVENTOR(S): Smith, Harold John; Mason, Peter; Ahmadi, Masoud; Nicholls, Paul Joseph; Greer, Valerie
PATENT ASSIGNEE(S): University College Cardiff Consultants Limited, UK
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001042181	A1	20010614	WO 2000-GB4700	20001208

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG .

PRIORITY APPLN. INFO.: GB 1999-29302 A 19991210
OTHER SOURCE(S): MARPAT 135:33380
GI



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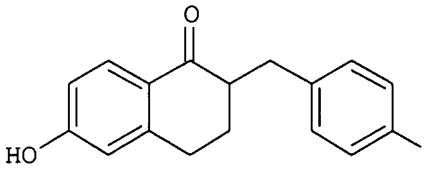

II

AB A benzyl tetralin I or a pharmaceutically acceptable salt or **prodrug** thereof is disclosed [wherein X = halogen, C1-6 alkyl (optionally substituted by at least one halogen), a fused bicyclic hydrophobic ring system, or Ph (optionally substituted by at least one halogen); Y = H or halogen; or X and Y together form the residue of a carbocyclic ring]. I are useful as inhibitors of 17β-hydroxy steroid dehydrogenase (17β-HSD) isoforms operable in the steroidogenesis pathway, and have therapeutic applications in the treatment of androgen- or estrogen-dependent or mediated diseases. In particular, I are useful for treating prostate cancer or breast cancer. I may be formulated with other steroidogenesis pathway enzyme inhibitors, where the inhibited enzyme is a 17β-HSD isoform, 5α-steroid reductase, aromatase P450arom, or estrogen sulfatase. Eight specific examples and their intermediates are described. For instance, 6-methoxy-3,4-dihydronaphthalen-1(2H)-one underwent a sequence of O-demethylation (57%), O-protection as the THP **ether** (86.8%), condensation with 4-chlorobenzaldehyde to give a 2-benzylidene derivative (51.7%), deprotection (94%), and hydrogenation of the benzylidene bond (69.5%), to give title compound II. This compound at 200 μM gave 97.9% inhibition of androstenedione reduction by human testicular microsomal 17β-HSD in vitro, and 59.6% inhibition of estrone reduction by human placental cytosolic 17β-HSD in vitro.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:557633 HCAPLUS
DOCUMENT NUMBER: 127:239118
TITLE: Drug delivery systems containing ester sunscreens and penetration enhancers
INVENTOR(S): Reed, Barry Leonard; Morgan, Timothy Matthias; Finnin, Barrie Charles
PATENT ASSIGNEE(S): Monash University, Australia; Reed, Barry Leonard; Morgan, Timothy Matthias; Finnin, Barrie Charles
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9729735	A1	19970821	WO 1997-AU91	19970219
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2244089	AA	19970821	CA 1997-2244089	19970219
AU 9717134	A1	19970902	AU 1997-17134	19970219
AU 706967	B2	19990701		
EP 901368	A1	19990317	EP 1997-904304	19970219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000504697	T2	20000418	JP 1997-528834	19970219
US 6299900	B1	20011009	US 1998-125436	19981218
AU 9952589	A1	19991202	AU 1999-52589	19991001
US 2002028235	A1	20020307	US 2001-910780	20010724
US 6818226	B2	20041116		
US 2004013620	A1	20040122	US 2003-428016	20030502
US 2004013621	A1	20040122	US 2003-428019	20030502
US 2004028625	A1	20040212	US 2003-428012	20030502
US 2004028725	A1	20040212	US 2003-428018	20030502
US 2004096405	A1	20040520	US 2003-636976	20030808
US 2004081684	A1	20040429	US 2003-644085	20030820
US 2004146469	A1	20040729	US 2004-759303	20040120
PRIORITY APPLN. INFO.:			AU 1996-8144	A 19960219
			AU 1997-17134	A3 19970219
			WO 1997-AU91	W 19970219
			US 1998-125436	A3 19981218
			US 2001-910780	A2 20010724

OTHER SOURCE(S): MARPAT 127:239118

AB A transdermal drug delivery system which comprises at least one physiol. active agent or **prodrug** thereof and at least one dermal penetration enhancer; characterized in that the dermal penetration enhancer is a safe skin-tolerant ester sunscreen. A non-occlusive, percutaneous or transdermal drug delivery system which comprises: (1) an effective amount of at least one physiol. active agent or **prodrug** thereof; (2) at least one non-volatile dermal penetration enhancer; and (3) at least one volatile liquid; characterized in that the dermal penetration enhancer is adapted to transport the physiol. active agent across a dermal surface or mucosal membrane of an animal, including a human, when the volatile liquid evaps., to form a reservoir or depot of a mixture comprising the penetration enhancer and the physiol. active agent or **prodrug** within said surface or membrane; and the dermal penetration enhancer is of low toxicity to, and is tolerated by, the dermal surface or mucosal membrane of the animal. The mean flux of 2% ketoprofen in 70% volume/volume aqueous ethanol through shed snakes kinetics in presence of 2% octyl salicylate in 70% volume/volume aqueous ethanol was 27.66 as compared to 2.58 μg/cm2.h for azone. A transdermal aerosol contained 17β-estradiol 2, octyl dimethyl-p-aminobenzoate 8, ethanol 69, and di-Me **ether** 30%.

L3 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:181570 HCAPLUS
DOCUMENT NUMBER: 124:233011
TITLE: Preparation of glycoside prodrugs with enhanced water solubility.
INVENTOR(S): Klemke, R.-Erich; Koreeda, Masato; Houston, Todd A.; Shull, Brian K.; Tuinman, Roeland J.
PATENT ASSIGNEE(S): Harrier, Inc., USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9532981	A1	19951207	WO 1995-US7027	19950601
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5693767	A	19971202	US 1994-251869	19940601
AU 9526617	A1	19951221	AU 1995-26617	19950601

PRIORITY APPLN. INFO.:

US 1994-251869	A	19940601
US 1991-644002	A2	19910122
US 1991-733915	B2	19910722
US 1992-815691	B2	19920124
US 1993-6447	B2	19930121
WO 1995-US7027	W	19950601

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Glycosides of aliphatic, alicyclic, aliphatic-aromatic, and aromatic aglycons having primary, secondary, or tertiary OH, SH, or CO2H groups with 2,3-dideoxy-α-D-erythrohex-2-enopyranoside fragments Q1-Q6 (A = acyl; X = O, S, CO2), were prepared Thus, a mixture of 4-acetamidophenol and hexaacetyl D-maltal was refluxed with iodine in THF for 12 h to give 30% of an α,β-glycoside, which was stirred with Ba(OH)2 in MeOH to give glycoside (I). I had 8 times the H2O solubility of tylenol itself in phosphate-buffered saline at pH 7.4.

L3 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:449157 HCAPLUS
DOCUMENT NUMBER: 117:49157
TITLE: Preparation of brain-targeted acyloxymethylphosphonate prodrugs
INVENTOR(S): Bodor, Nicholas S.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 179 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

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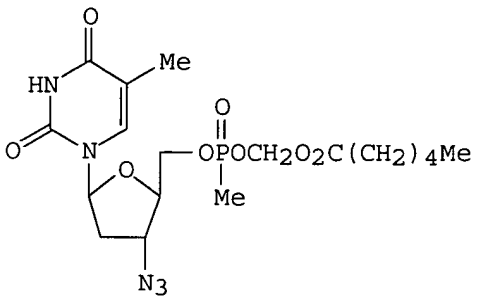
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9200988	A1	19920123	WO 1991-US4824	19910712
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MN, MW, NL, NO, PL, RO, SD, SE, SU				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
US 5177064	A	19930105	US 1990-553548	19900713
CA 2087194	AA	19920114	CA 1991-2087194	19910712
AU 9183000	A1	19920204	AU 1991-83000	19910712
AU 649466	B2	19940526		
EP 539493	A1	19930505	EP 1991-913701	19910712
EP 539493	B1	19970326		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05509313	T2	19931222	JP 1991-513064	19910712
AT 150759	E	19970415	AT 1991-913701	19910712
US 5413996	A	19950509	US 1992-962504	19921016
US 5618803	A	19970408	US 1994-340896	19941115

PRIORITY APPLN. INFO.: US 1990-553548 A 19900713
WO 1991-US4824 A 19910712
US 1992-962504 A3 19921016

OTHER SOURCE(S): MARPAT 117:49157
GI



II

AB QP(O)(R1)OCHR2O2CR3 [Q = O-bonded drug moiety; R1 = alkyl, aryl, aralkyl; R2 = H, hetero)aryl, (cyclo)alkyl, heterocyclyl, aralkyl; R3 = alkyl, alkenyl, (alkyl)cycloalkyl(alkyl), aryloxyalkyl, pyridyl, (substituted) Ph, phenylalkyl], were prepared Thus, zidovudine was stirred with MeP(O)Cl2 and Na2CO3 in acetone for 17 h; H2O was added to give 31.3% zidovudine methylphosphonate (I), which was treated with iodomethyl hexanoate and CsF in DMF to give title compound II. Title compds. are rapidly hydrolyzed in vivo, and I was found in the brain after administration of II.

L3 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:7383 HCAPLUS
DOCUMENT NUMBER: 112:7383
TITLE: Preparation of dihydropyridine-containing prodrugs for brain-specific drug delivery
INVENTOR(S): Bodor, Nicholas S.
PATENT ASSIGNEE(S): University of Florida, USA

SOURCE: U.S., 282 pp. Cont.-in-part of U.S. 4,479,932.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4824850	A	19890425	US 1984-665940	19841029
US 4479932	A	19841030	US 1982-379316	19820518
US 4622218	A	19861111	US 1983-475493	19830315
EP 218300	A2	19870415	EP 1986-201710	19830512
EP 218300	A3	19880928		
R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE				
EP 221588	A2	19870513	EP 1986-201711	19830512
EP 221588	A3	19880921		
R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE				
EP 222425	A2	19870520	EP 1986-201714	19830512
EP 222425	A3	19880921		
R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE				
EP 224283	A2	19870603	EP 1986-201713	19830512
EP 224283	A3	19880921		
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EP 256577	A2	19880224	EP 1987-201385	19830512
EP 256577	A3	19880706		
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EP 262696	A2	19880406	EP 1987-201384	19830512
EP 262696	A3	19880720		
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CA 1253856	A1	19890509	CA 1983-428192	19830516
ZA 8303521	A	19841224	ZA 1983-3521	19830517
US 4540564	A	19850910	US 1983-516382	19830722
US 4727079	A	19880223	US 1985-733463	19850513
US 4880921	A	19891114	US 1987-75830	19870720
US 4900837	A	19900213	US 1987-76191	19870721
EP 334853	A1	19891004	EP 1987-907186	19871013
EP 334853	B1	19930609		
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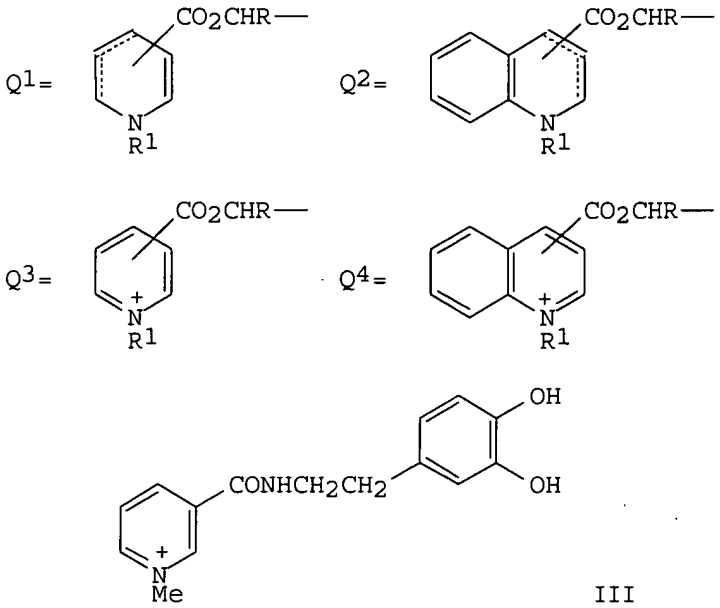
AT 90355	E	19930615	AT 1987-907186	19871013
US 4880816	A	19891114	US 1987-116583	19871104
US 5008257	A	19910416	US 1989-295938	19890111
US 5187158	A	19930216	US 1991-639283	19910110
US 5525727	A	19960611	US 1992-967979	19921028

PRIORITY APPLN. INFO.:		
US 1982-379316	A2	19820518
US 1983-461543	A2	19830127
US 1983-475493	A2	19830315
CA 1983-428192	A	19830516
US 1983-516382	A2	19830722
JP 1982-101940	A	19820614
EP 1983-902034	P	19830512
WO 1983-US725	A	19830512
WO 1983-WO725	A	19830512
ES 1983-522489	A	19830517
IE 1983-1149	A	19830517
ZA 1983-3521	A	19830517
IT 1983-48327	A	19830518
US 1984-665940	A2	19841029
US 1985-733463	A3	19850513

EP 1987-907186 A 19871013
WO 1987-US2590 A 19871013
US 1989-295938 A3 19890111
US 1991-639283 A3 19910110
OTHER SOURCE(S): CASREACT 112:7383; MARPAT 112:7383
GI



III

AB Compds. of the formula D(DHC)n (I) [D = residue of a centrally acting drug having anticonvulsant, sedative and/or hypnotic properties, said drug being a hydantoin or barbiturate or an analog of a hydantoin or barbiturate, said drug containing at least one reactive amide or imide functional group, said residue being characterized by the absence of a H atom from at least one of said amide or imide functional groups in said drug; n = pos. integer equal to the number of said functional groups from which a H atom is absent; DHC = reduced, biooxidizable, blood-brain barrier penetrating, lipoidal form of a dihydropyridine-pyridinium salt redox carrier; DHC = Q1, Q2, etc.; R = H, C1-7 alkyl, C3-8 cycloalkyl, C1-7 haloalkyl, etc.; R1 = C1-7 alkyl, haloalkyl, C7-10 aralkyl; dotted line indicates the presence of a double bond in position 4 or 5 of the dihydropyridine ring or position 2 or 3 of the dihydroquinoline ring] were prepared as brain-specific prodrugs. Quaternary salts of the formula D(QC+)nqX-t (II) (D = as given above; X- = anion of a pharmaceutically acceptable organic or inorg. acid; t = valence of acid anion; q = number which when multiplied by t is equal to n; QC+ = hydrophilic, ionic pyridinium salt form of a dihydropyridine-pyridinium salt redox carrier; QC+ = Q3, Q4, etc.; R, R1 = as given above; n = pos. integer equal to the number of said functional groups from which a H atom is absent) were prepared as intermediates for I. Reaction of 5,5-diphenyl-3-hydroxymethyl-2,4-imidazolidinedione with nicotinic anhydride, followed by methylation with MeI and reduction, gave 5,5-diphenyl-3-[(1'-methyl-1',4'-dihydropyridin-3'-yl)carbonyloxymethyl]-2,4-imidazolidinedione. After one single injection of 1-methyl-3-[[N-[β-(3,4-dipivalyloxyphenyl)ethyl]]carbamoyl-1,4-dihydropyridine to a rat, the pyridinium compound III could be seen to appear and then to disappear quickly from the blood, with a half-life of

27 min. On the contrary, the concentration of III increases in the brain steadily, reaching a maximum at about 30 min following administration. For III, the half-life of diappearance from the brain is about 3.2 h.

=> d his

(FILE 'HOME' ENTERED AT 16:42:20 ON 26 APR 2005)

FILE 'STNGUIDE' ENTERED AT 16:42:25 ON 26 APR 2005

FILE 'HCAPLUS' ENTERED AT 16:42:37 ON 26 APR 2005
L1 57193 S TESTOSTERONE
L2 48 S L1 AND PRODRUG
L3 6 S L2 AND ETHER
L4 17 S L2 AND ESTER

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L2 ANSWER 1 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:283298 HCAPLUS
TITLE: Combinations of chlorpromazine compounds and antiproliferative drugs for the treatment of neoplasms
INVENTOR(S): Lee, Margaret S.; Nichols, James M.; Zhang, Yanzhen; Keith, Curtis
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027842	A2	20050331	WO 2004-US30368	20040916

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-504310P P 20030918
AB The invention discloses a method for treating a patient having a cancer or other neoplasm by administering chlorpromazine or a chlorpromazine analog and an antiproliferative agent simultaneously or within 14 days of each other in amts. sufficient to treat the patient.

L2 ANSWER 2 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:52993 HCAPLUS
DOCUMENT NUMBER: 142:190557
TITLE: Antitumor activity of methoxymorpholinyl doxorubicin: Potentiation by cytochrome P450 3A metabolism
AUTHOR(S): Lu, Hong; Waxman, David J.

09872705

CORPORATE SOURCE: Division of Cell and Molecular Biology, Department of Biology, Boston University, Boston, MA, USA
SOURCE: Molecular Pharmacology (2005), 67(1), 212-219
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Methoxymorpholinyl doxorubicin (MMDX) is a novel liver cytochrome P 450 (P 450)-activated anticancer **prodrug** whose toxicity toward cultured tumor cells can be potentiated up to 100-fold by incubation with liver microsomes and NADPH. In the present study, a panel of human liver microsomes activated MMDX with potentiation ratios directly correlated to the CYP3A-dependent **testosterone** 6β-hydroxylase activity of each liver sample. Microsome-activated MMDX exhibited nanomolar IC50 values in growth-inhibition assays of human tumor cell lines representing multiple tissues of origin: lung (A549 cells), brain (U251 cells), colon (LS180 cells), and breast (MCF-7 cells). Anal. of individual cDNA-expressed CYP3A enzymes revealed that rat CYP3A1 and human CYP3A4 activated MMDX more efficiently than rat CYP3A2 and that human P450s 3A5 and 3A7 displayed little or no activity. MMDX cytotoxicity was substantially increased in Chinese hamster ovary cells after stable expression of CYO3A4 in combination with P 450 reductase. CYP3A activation of MMDX abolished the parent drug's residual cross-resistance in a doxorubicin-resistant MCF-7 cell line that overexpresses P-glycoprotein. CYP3A-activated MMDX displayed a comparatively high intrinsic stability, with a t1/2 of .apprx.5.5 h at 37°. MMDX was rapidly activated by CYP3A at low (.apprx.1-5 nM) **prodrug** concns., with 100% tumor cell kill obtained after as short as a 2-h exposure to the activated metabolite. These findings demonstrate that MMDX can be activated by CYP3A metabolism to a potent, long-lived, and cell-permeable cytotoxic metabolite and suggest that this anthracycline **prodrug** may be used in combination with CYP3A4 in a P 450 **prodrug** activation-based gene therapy for cancer treatment.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:934160 HCAPLUS
DOCUMENT NUMBER: 141:388650
TITLE: Anti-CD74 immunoconjugates and their therapeutic and diagnostic uses
INVENTOR(S): Griffiths, Gary L.; Hansen, Hans J.; Goldenberg, David M.; Lundberg, Bo B.
PATENT ASSIGNEE(S): Immunomedics, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 44 pp., Cont.-in-part of U.S. Ser. No. 377,122.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004219203	A1	20041104	US 2003-706852	20031112
US 6306393	B1	20011023	US 1999-307816	19990510
US 2002071807	A1	20020613	US 2001-965796	20011001
US 2003124058	A1	20030703	US 2002-314330	20021209

US 2003133930	A1	20030717	US 2003-350096	20030124
US 2004115193	A1	20040617	US 2003-377122	20030303
WO 2004110390	A2	20041223	WO 2004-US19238	20040617

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:	US 1999-307816	A1 19990510
	US 2000-590284	A1 20000609
	US 2001-965796	A1 20011001
	US 2002-360259P	P 20020301
	US 2002-314330	A2 20021209
	US 2003-350096	A2 20030124
	US 2003-377122	A2 20030303
	US 2003-478830P	P 20030617
	US 1997-41506P	P 19970324
	US 1998-38995	A2 19980312
	US 1999-138284P	P 19990609
	US 2003-706852	A 20031112

AB Disclosed are compns. that include anti-CD74 immunoconjugates and a therapeutic and/or diagnostic agent. Also disclosed are methods for preparing the immunoconjugates and using the immunoconjugates in diagnostic and therapeutic procedures. The compns. may be part of a kit for administering the anti-CD74 immunoconjugates compns. in therapeutic and/or diagnostic methods. Anti-CD74 binding mols. are conjugated to the one or more lipids by one or more of a sulfide linkage, a hydrazone linkage, a hydrazine linkage, an ester linkage, an amido linkage, an amino linkage, an imino linkage, a thiosemicarbazone linkage, a semicarbazone linkage, an oxime linkage, a carbon-carbon linkage. Anti-CD74 immunoconjugates comprise a drug, a **prodrug**, a toxin, an enzyme, a radioisotope, an immunomodulator, a cytokine, a hormone, an antibody., an oligonucleotide, or a photodynamic agent.

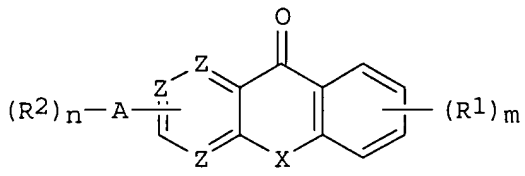
L2 ANSWER 4 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2004:817876 HCAPLUS
DOCUMENT NUMBER:	141:314155
TITLE:	Preparation of xanthenone and acridinone DNA-PK inhibitors as cancer treatment potentiators
INVENTOR(S):	Halbrook, James W.; Kesicki, Edward A.; Burgess, Laurence Edward; Schlachter, Stephen T.; Eary, Charles T.; Schiro, Justin G.
PATENT ASSIGNEE(S):	Icos Corporation, USA
SOURCE:	PCT Int. Appl., 149 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004085418	A2	20041007	WO 2004-US8459	20040319

WO 2004085418 A3 20050127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2003-456999P P 20030324
OTHER SOURCE(S): MARPAT 141:314155
GI



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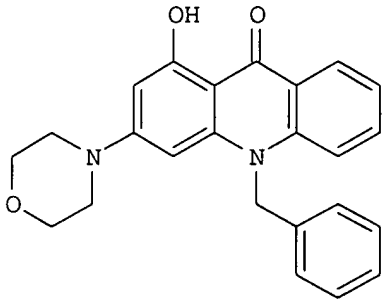

II

AB Title compds. I [wherein m = 0-3; n = 0-4; X = O, SO0-2, NRa; Z = independently CRb, N; A = heteroaryl; R1 = independently halo (un)substituted (cyclo)alkyl, heterocyclylalkyl, amino carboxy, phosphoryl, acyl, (hetero)aryl, etc.; R2 = independently halo, CHO, (un)substituted alkyl, (hetero)aryl, carbamoyl, carboxy, etc.; R1 = H, (cyclo)alkyl, (hetero)aryl, carboxy, carbamoyl, etc.; Rb = independently H, alkyl, halo, CHO, alkoxy, phosphoryl, amino, carboxy, etc.; and pharmaceutically acceptable salts and prodrugs thereof] were prepared as DNA-dependent protein kinase (DNA-PK) inhibitors. I and their pharmaceutical compns. potentiate cancer treatment by sensitizing cells to an agent that induces DNA lesions. For example, condensation of 1,3-dihydroxy-10H-acridin-9-one with trifluoromethanesulfonic anhydride gave the triflate. Pd-catalyzed substitution of the monoester with morpholine, followed by benzylation provided II. The latter inhibited DNA-PK induced phosphorylation of a p53 peptide substrate with a IC50 of 20 nM.

L2 ANSWER 5 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:606359 HCAPLUS
DOCUMENT NUMBER: 141:134689
TITLE: Method of achieving accelerated fat loss by

administration of 7-oxo-DHEA or a **prodrug** to a dieting mammal
INVENTOR(S): Zenk, John L.
PATENT ASSIGNEE(S): Humanetics Corporation, USA
SOURCE: PCT Int. Appl., 6 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004062606	A2	20040729	WO 2004-US541	20040112
WO 2004062606	A3	20041125		

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ

PRIORITY APPLN. INFO.: US 2003-439816P P 20030113
AB Accelerating fat loss by administering to a dieting mammal the fat loss accelerating agent 7-oxo-DHEA or a pro-drug thereof incapable of in vivo conversion to **testosterone.**

L2 ANSWER 6 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:569865 HCAPLUS
DOCUMENT NUMBER: 141:82949
TITLE: Method of modulating the basal metabolic rate of a dieting mammal by administration of a metabolic modulating agent to the dieting mammal
INVENTOR(S): Zenk, John
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 3 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004138303	A1	20040715	US 2003-340980	20030113
JP 2004217657	A2	20040805	JP 2004-4160	20040109
EP 1437138	A1	20040714	EP 2004-543	20040113

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.: US 2003-340980 A 20030113
AB Modulating the metabolism of a dieting mammal by administering to the dieting mammal the metabolic modulating agent 7-oxo DHEA or a pro-drug thereof incapable of in vivo conversion to **testosterone.**

L2 ANSWER 7 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:355044 HCAPLUS
DOCUMENT NUMBER: 140:350597
TITLE: Treating androgen decline in aging male (ADAM)-associated conditions with selective androgen

receptor modulators (SARMs)
INVENTOR(S): Dalton, James T.; Miller, Duane D.; Steiner, Mitchell S.; Veverka, Karen A.
PATENT ASSIGNEE(S): GTX, Inc., USA
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004035739	A2	20040429	WO 2003-US32513	20031014
WO 2004035739	A3	20040930		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
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US 2005080054	A1	20050414	US 2003-683161	20031014

PRIORITY APPLN. INFO.: US 2002-418336P P 20021016
OTHER SOURCE(S): MARPAT 140:350597

AB The invention provides a method for treating, preventing, suppressing, inhibiting or reducing the incidence of an androgen decline in aging male (ADAM)-associated condition in a male subject, by administering to the subject a selective androgen receptor modulator (SARM) compound and/or its analog, derivative, isomer, metabolite, pharmaceutically acceptable salt, pharmaceutical product, hydrate, N-oxide, **prodrug**, polymorph, crystal, or any combination thereof. The invention further provides a method of treating, preventing, suppressing, inhibiting or reducing the incidence of sexual dysfunction, decreased sexual libido, erectile dysfunction, hypogonadism, sarcopenia, osteopenia, osteoporosis, alterations in cognition and mood, depression, anemia, hair loss, obesity, benign prostate hyperplasia or prostate cancer due to ADAM in a male subject, by administering to the subject a SARM compound and/or its analog, derivative, isomer, metabolite, pharmaceutically acceptable salt, pharmaceutical product, hydrate, N-oxide, **prodrug**, polymorph, crystal, or any combination thereof.

L2 ANSWER 8 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:220151 HCAPLUS
DOCUMENT NUMBER: 140:270858
TITLE: Preparation of heterocyclic aromatic compounds useful as growth hormone secretagogues
INVENTOR(S): Yu, Guixue; Li, Jun; Ewing, William R.; Sulsky, Richard B.; Li, James J.; Tino, Joseph A.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 193 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004021984	A2	20040318	WO 2003-US27513		20030902
WO 2004021984	A3	20041125			

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004147568	A1	20040729	US 2003-653410		20030902
PRIORITY APPLN. INFO.:			US 2002-408099P	P	20020904
			US 2003-491645P	P	20030731

OTHER SOURCE(S): MARPAT 140:270858

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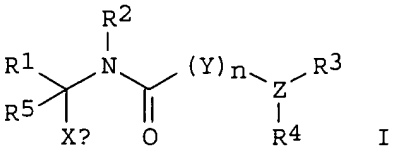

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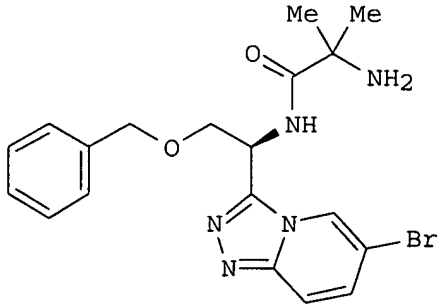


II

AB Title compds. I [R1 = (un)substituted alkyl, aryl, alkenyl, alkynyl, etc.; R2, R3 and R4 independently = H, (un)substituted alkyl, aryl, alkenyl, arylalkyl, heterocycle, etc.; or R3 and R4 together form a 3-8 membered cycloalkyl or heterocyclic ring; or one or more of R3 and R4 together with one or more of Y and Z form a mono or bicyclic cycloalkyl or heterocyclic ring; R5 = H, (un)substituted alkyl, cycloalkyl, heterocycle, aryl and heteroaryl; Y = linking group consisting of (un)substituted alkylene, alkenylene, alkynylene, arylene, and heteroarylene; n = integer from 1-6; Z = N; Xa = 2 to 4 fused or spiro cycloalkyl, heterocycle, aryl or heteroaryl rings wherein one or more of said rings may be optionally substituted with 1-5 substituents of Ra or Rb; Ra and Rb independently = CN, CO, halo, alkyl, alkenyl, alkynyl, arylalkyl, etc.] and their methods of preparation are provided that are useful in stimulating endogenous production or release of growth hormone (no data). Thus, e.g., II·HCl was prepared via amidation of 3-benzyloxy-2-tert-butoxycarbonylaminopropionic acid with 5-bromopyridin-2-yl hydrazine and subsequent cyclocondensation with trimethylsilyl azide, deprotection, amidation with 2-tert-butoxycarbonylamino-2-methylpropionic acid, deprotection and conversion to HCl derivative with acid washing. The compds. provided herein are claimed as useful in treating obesity, osteoporosis (improving bone d.) and in improving muscle mass and muscle strength.

L2 ANSWER 9 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:836591 HCAPLUS
DOCUMENT NUMBER: 139:333131
TITLE: Methods for improving efficacy of treatment with growth hormone secretagogues
INVENTOR(S): Fryburg, David A.; Taylor, Ann E.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 25 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003199514	A1	20031023	US 2003-392527		20030320
PRIORITY APPLN. INFO.:			US 2002-368455P	P	20020327

OTHER SOURCE(S): MARPAT 139:333131
AB The present invention provides methods of increasing efficacy of treatment with growth hormone secretagogues, prodrugs thereof and pharmaceutically acceptable salts of said secretagogues and said prodrugs, for patients who have normal or above normal levels of **testosterone.** The present invention also provides methods of reducing the therapeutic doses of such compds. in such patients. More specifically, the present invention provides such methods wherein the growth hormone secretagogues are (I: HETCOC(R3)(R4)N(X4)COR6N(R7)R8 wherein [HET = heterocycle; R3 = (C1-C10)alkyl, etc.; R4 = H, (C1-C6)alkyl, (C3-C7)cycloalkyl; or R3 and R4 form (C5-C7)cycloalkyl, etc.; X4 = H, (C1-C6)alkyl; or X4 and R4 form 5-7-member ring; R6 = bond, -Z1(CH2)aC(X)5(X5a)(CH2)b-, etc.; a, b = 0-3; X5, X5a = H, CF3, etc.; Z1 = bond, O, NX2, provided that when a and b are both 0 then Z1 is not NX2 or O; R7 and R8 = H, (substituted)(C1-C6)alkyl, etc.]), a **prodrug** thereof or a pharmaceutically acceptable salt of said secretagogue or said **prodrug.** In a double-blind, placebo-controlled, multiple dose evaluation of 2-amino-N-[2-[3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydropyrazolo[4,3-c]pyridin-5-yl]-1-(R)-benzyloxymethyl-2-oxoethyl]isobutyramide, L-tartrate in calorically restricted obese men and women, **testosterone** level appeared to influence the response to growth hormone secretagogue.

L2 ANSWER 10 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:117794 HCAPLUS
DOCUMENT NUMBER: 138:153537
TITLE: Preparation of imidazole-containing heterobicyclic modulators of androgen receptor function
INVENTOR(S): Sun, Chongqing; Robl, Jeffrey A.; Salvati, Mark E.; Wang, Tammy; Hamann, Lawrence; Augeri, David
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003011824	A1	20030213	WO 2002-US24185	20020731

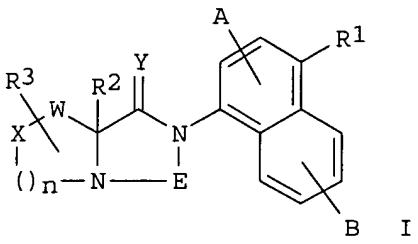
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG

US 2003055094	A1	20030320	US 2002-209461	20020731
US 6670386	B2	20031230		
EP 1414795	A1	20040506	EP 2002-756813	20020731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2004092559	A1	20040513	US 2003-685020	20031014
PRIORITY APPLN. INFO.:			US 2001-309059P	P 20010731
			US 2002-209461	A3 20020731
			WO 2002-US24185	W 20020731

OTHER SOURCE(S): MARPAT 138:153537

GI



I

AB The invention provides imidazole-containing heterobicyclic compds. (shown as I, including all **prodrug** esters, pharmaceutically acceptable salts and stereoisomers thereof; variables defined below; e.g. tetrahydro-2-(4-nitro-1-naphthalenyl)imidazo[1,5-a]pyridine-1,3(2H,5H)-dione), methods of using such compds. for the treatment of nuclear hormone receptor-associated conditions, such as age related diseases, for example sarcopenia, and pharmaceutical compns. containing such compds. Pharmacol. assay procedures are described but results for I are not reported. For I: R1 = H, cyano, nitro, halo, heterocyclo, OR4, CO2R5, CONHR5, COR5, S(O)mR5, SO2NR5R5', NHCOR5 and NHSO2R5; R2 = H, alkyl or substituted alkyl, (un)substituted alkenyl, (un)substituted arylalkyl, CO2R5, CONR5R5' and CH2OR5; R3 = H, (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, (un)substituted cycloalkyl, (un)substituted arylalkyl, (un)substituted heterocycloalkyl, (un)substituted aryl, (un)substituted heteroaryl, halo, cyano, NHCOR5, NHCO2R5, NHCONR5R5', NHSO2R5 and OR4. R4 = H, (un)substituted alkyl, CHF2, CF3 and COR5; R5 and R5' = H, (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, (un)substituted cycloalkyl, (un)substituted heterocycloalkyl, (un)substituted arylalkyl, (un)substituted aryl, (un)substituted heteroaryl and cyano; W = (CR6R6')m, CHOH(CR6R6')m, CO(CR6R6')m and C:NOR4(CR6R6')m. R6 and R6' = H, (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, (un)substituted cycloalkyl, (un)substituted arylalkyl, (un)substituted heterocycloalkyl, (un)substituted aryl, (un)substituted heteroaryl, halo, cyano, NHCOR5, NHCO2R5, NHCONR5R5', NHSO2R5 and OR4; X = methylene, O, S(O)m, NCOR5,

NCO2R5, NCONHR5R5', NSO2NR5R5'; Y = O, S and H2; E = C:Z, CHR5, SO2, P(O)R5 and P(O)OR5; Z = O, S, NH and NR5; A and B = H, halo, cyano, nitro, (un)substituted alkyl and OR4; m = 0-2; and n = 1-2;. Although the methods of preparation are not claimed, 42 example prepns. are included.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:977668 HCAPLUS
DOCUMENT NUMBER: 138:61309
TITLE: Enhanced steroidal drug delivery in transdermal systems
INVENTOR(S): Houze, David; Nguyen, Viet
PATENT ASSIGNEE(S): Noven Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102390	A1	20021227	WO 2002-US16579	20020618
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1406633	A1	20040414	EP 2002-749537	20020618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002010516	A	20041005	BR 2002-10516	20020618
JP 2005500299	T2	20050106	JP 2003-504976	20020618
US 2003152613	A1	20030814	US 2002-330279	20021230
US 2003152614	A1	20030814	US 2002-330360	20021230
US 2003152615	A1	20030814	US 2002-330361	20021230
US 2003232073	A1	20031218	US 2002-330281	20021230
PRIORITY APPLN. INFO.:			US 2001-298381P	P 20010618
			US 2001-948107	A 20010907
			WO 2002-US16579	W 20020618

AB A composition for transdermal administration resulting from an admixt. includes a therapeutically effective amount of a drug that includes a parent drug and a **prodrug** and a carrier, wherein the parent drug and **prodrug** are individually present in an amount sufficient for a pharmacol. effect. The admixt. include: a therapeutically effective amount of a steroid and a steroid derivative and a carrier for the steroid. The steroid and the corresponding derivative are present in a weight ratio of 10:1 to 1:10 steroid-corresponding steroid derivative In a preferred embodiment ratio is 6:1 to 1:6. In a preferred embodiment, the corresponding steroid derivative is a steroidal ester. In another preferred embodiment, the carrier is a polymer that includes a pressure-sensitive adhesive. In another preferred embodiment, the parent drug is an ACE inhibitor such as ramipril

and the **prodrug** is an ACE inhibitor **prodrug** such as ramipril Et and/or Me esters. Thus, a transdermal delivery system contained norethindrone 1.2, estradiol 0.9, norethindrone acetate 2.5, VA-64 15.0, GMS-737 (acrylic PSA), oleic acid 3.0, dipropylene glycol 9.0, and Bio-PSA-7-4603 63.4%.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:883250 HCAPLUS
DOCUMENT NUMBER: 139:78567
TITLE: Adenovirus Mediated Prostate Specific Enzyme **Prodrug** Gene Therapy Using Prostate Specific Antigen Promoter Enhanced by the Cre-loxP System
AUTHOR(S): Yoshimura, Ichiro; Ikegami, Shusei; Suzuki, Satoshi; Tadakuma, Takushi; Hayakawa, Masamichi
CORPORATE SOURCE: Departments of Urology and Parasitology and Immunology, National Defense Medical College, Tokorozawa, Saitama, Japan
SOURCE: Journal of Urology (Hagerstown, MD, United States) (2002), 168(6), 2659-2664
CODEN: JOURAA; ISSN: 0022-5347
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB PURPOSE: Tissue or tumor specific gene delivery is crucial for achieving successful results in suicide gene therapy. Prostate specific antigen (PSA) promoter is known to be highly specific in prostate tissue but its promoter activity is much weaker than that of constitutive viral promoters. In the current study we enhanced PSA promoter activity by combining it with the Cre-loxP system. We also applied this system to adenovirus mediated suicide gene therapy with the cytosine deaminase (CD) gene. MATERIALS AND METHODS: The Cre-loxP DNA recombination system was used to enhance PSA promoter. A plasmid with the PSA promoter-enhancer combination was constructed to drive Cre recombinase. Another plasmid contained the cytomegalovirus promoter-loxP-flanked stop signal-luciferase gene. LNCaP human prostate cancer cells were co-transfected with these 2 plasmids and luciferase activity was measured to assess promoter activities. Adenoviral vectors with the CD suicide gene were constructed in similar fashion and tested in LNCaP cells in in vitro/in vivo prostate cancer models. RESULTS: Promoter activity of the combined PSA promoter/enhancer and Cre-loxP system was 3 times stronger than that of PSA promoter/enhancer alone. It was further enhanced 7-fold in the presence of **testosterone.** Application of this system to CD suicide gene therapy by adenoviral vectors inhibited s.c. LNCaP tumor growth in nude mice. CONCLUSIONS: Combining the Cre-loxP system with PSA promoter/enhancer amplified promoter activity and was found to inhibit the growth of PSA producing prostate cancer cells in vivo.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:551606 HCAPLUS
DOCUMENT NUMBER: 137:99033
TITLE: Water soluble amine esters of **testosterone** for intranasal administration
INVENTOR(S): Hussain, Anwar A.
PATENT ASSIGNEE(S): University of Kentucky, USA
SOURCE: U.S., 8 pp.

CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6423701	B1	20020723	US 1996-591767	19960125

PRIORITY APPLN. INFO.: US 1996-591767 19960125
OTHER SOURCE(S): MARPAT 137:99033

AB The present invention provides novel water soluble **testosterone** analogs. These **testosterone** analogs are suitable for intranasal administration to patients requiring increased plasma **testosterone** levels. The present invention also provides pharmaceutical compns. containing the **testosterone** analogs of the present invention. The present invention further provides a method of increasing plasma **testosterone** levels in patients in need of such treatment comprising the intranasal administration of the water-soluble **testosterone** analogs and pharmaceutical compns. of the present invention.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:426631 HCAPLUS
DOCUMENT NUMBER: 137:16062
TITLE: Combination for treating andropause and related conditions containing estrogen agonists/antagonists and **testosterone**
INVENTOR(S): McLean, David Burton
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 43 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1210951	A2	20020605	EP 2001-309457	20011108
EP 1210951	A3	20030924		
EP 1210951	B1	20050202		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
AT 288303	E	20050215	AT 2001-309457	20011108
US 2002115676	A1	20020822	US 2001-995130	20011127
CA 2363935	AA	20020530	CA 2001-2363935	20011128
AU 2001095165	A5	20020606	AU 2001-95165	20011129
ZA 2001009836	A	20030529	ZA 2001-9836	20011129
NZ 515822	A	20030530	NZ 2001-515822	20011129
JP 2002193809	A2	20020710	JP 2001-365803	20011130

PRIORITY APPLN. INFO.: US 2000-250071P P 20001130
OTHER SOURCE(S): MARPAT 137:16062
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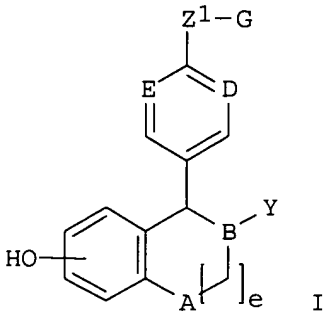

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AB The present invention concerns the treatment of andropause and related conditions using a combination of an estrogen agonist/antagonist and **testosterone.** The Markush structure for the estrogen agonist/antagonist is I, where A = CH2 or NR; B, D, and E = CH or N; Y= a ring; Z1 is linear or part of a ring with G; and G is a linear or a ring. The specifically claimed estrogen agonist/antagonist is (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-ylethoxy)phenyl]-5,6,7,8-tetrahydronaphthalene-2-ol or an optical or geometric isomer thereof; a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a **prodrug** thereof. Drugs containing the compds. of the invention can be used to treat gynecomastia, lipid disorders, cardiovascular disease, atherosclerosis, hypogonadism, benign prostatic hyperplasia, or osteoporosis; or increasing libido; or maintaining or improving vascular reactivity in a male patient. A treatment kit containing (a) one or more pharmaceutical compns. comprising an estrogen agonist/antagonist and **testosterone**; and (b) instructions for administering the pharmaceutical composition is also claimed.

L2 ANSWER 15 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:314394 HCAPLUS
DOCUMENT NUMBER: 136:335264
TITLE: Use of an estrogen agonists and antagonists for assessment, improvement, or maintenance of urogenital health
INVENTOR(S): Day, Wesley Warren; Lee, Andrew George; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 52 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1199069	A2	20020424	EP 2001-308625	20011009
EP 1199069	A3	20031119		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CA 2358938	AA	20020416	CA 2001-2358938	20011012
US 2002128276	A1	20020912	US 2001-976825	20011012
JP 2002179593	A2	20020626	JP 2001-316248	20011015
ZA 2001008443	A	20030415	ZA 2001-8443	20011015

NZ 514821	A	20040130	NZ 2001-514821	20011015
US 2003125319	A1	20030703	US 2002-292203	20021112
PRIORITY APPLN. INFO.:			US 2000-240789P	P 20001016
			US 2001-976825	A3 20011012

OTHER SOURCE(S): MARPAT 136:335264

AB The invention relates to methods and kits useful for the improvement, or maintenance urogenital health using an estrogen agonist/antagonist compds. (Markush structures are included). The methods of treatment are effective for improving or maintaining urogenital health while substantially reducing the concomitant liability of adverse effects associated with estrogen administration. This invention also relates to methods of assessing vaginal health.

L2 ANSWER 16 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:248837 HCAPLUS
DOCUMENT NUMBER: 137:299709
TITLE: **Testosterone** 17β-N,N-dimethylglycinate hydrochloride: a **prodrug** with a potential for nasal delivery of **testosterone**
AUTHOR(S): Hussain, Anwar A.; Al-Bayatti, Ansam A.; Dakkuri, Adnan; Okochi, Kazuhiro; Hussain, Munir A.
CORPORATE SOURCE: College of Pharmacy, University of Kentucky, Lexington, KY, 40536-0082, USA
SOURCE: Journal of Pharmaceutical Sciences (2002), 91(3), 785-789
CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of this study was to examine the potential of the nasal route for the systemic delivery of the poorly water-soluble drug **testosterone** (TS) using a water-soluble **prodrug**, TS 17β-N,N-dimethylglycinate hydrochloride. The physicochem. properties of the **prodrug**, in vitro hydrolysis in human liver homogenate, and in vivo nasal and i.v. expts. were performed in rats. The aqueous solubility of the **prodrug** was more than 100 mg/mL, compared with 0.01 mg/mL for TS, and its log partition coefficient between 0.05 M, phosphate buffer (pH 6) and octanol was 2.4. The **prodrug** was found to generate TS in 33% human liver homogenate and was absorbed from the nasal cavity rapidly and quant. The bioavailabilities of both the **prodrug** and TS after nasal administration of the **prodrug** were similar to that after equivalent i.v. doses. These studies in rats suggest that this water-soluble **prodrug** of TS may have therapeutic utility for the management of TS deficiency.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 17 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:885822 HCAPLUS
DOCUMENT NUMBER: 136:25103
TITLE: Sulfonamide group-containing pharmaceutical prodrugs
INVENTOR(S): Elger, Walter; Hillisch, Alexander; Hedden, Annemarie; Schwarz, Sigfrid; Schoellkopf, Klaus
PATENT ASSIGNEE(S): Jenapharm GmbH & Co. KG, Germany
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001091797	A2	20011206	WO 2001-EP5169	20010508
WO 2001091797	A3	20020620		
W: AE, AG, AU, BA, BB, BG, BR, CA, CN, CO, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LS, MA, MG, MN, MX, NO, NZ, PL, SG, SK, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10027887	A1	20011213	DE 2000-10027887	20000531
CA 2410630	AA	20021128	CA 2001-2410630	20010508
EP 1294402	A2	20030326	EP 2001-943329	20010508
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
BR 2001011294	A	20030610	BR 2001-11294	20010508
JP 2003534386	T2	20031118	JP 2001-587809	20010508
NO 2002005739	A	20021129	NO 2002-5739	20021129
BG 107556	A	20040130	BG 2003-107556	20030214
US 2004014781	A1	20040122	US 2003-296973	20030801
PRIORITY APPLN. INFO.:			DE 2000-10027887 A	20000531
			WO 2001-EP5169 W	20010508

OTHER SOURCE(S): MARPAT 136:25103

AB The invention relates to compds. which, acting as a **prodrug** and/or support, enable an active agent to be taken up by the erythrocytes and/or an active agent to bind to the erythrocytes. The uptake of these compds. by and/or the binding thereof to the erythrocytes is made possible by a group of formula -SO2NR1R2, wherein R1 and R2, independently of each other, is H, acyl, alky, cycloalkyl group, aryl, cyano or a hydroxy group. The inventive prodrugs enable active agents such as endogenic substances, natural substances and synthetic substances with therapeutically useful properties which have a high "first path" effect, to be administered orally effectively or significantly improve the oral activity. The sepharose-immobilized estradiol sulfamate was found to bind to carbonic anhydrase II in erythrocytes.

L2 ANSWER 18 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:845768 HCAPLUS
DOCUMENT NUMBER: 137:68023
TITLE: **Testosterone** delivery using glutamide-based complex high axial ratio microstructures
AUTHOR(S): Goldstein, Alex S.; Amory, John K.; Martin, Stephanie M.; Vernon, Chris; Matsumoto, Alvin; Yager, Paul
CORPORATE SOURCE: Departments of Chemistry and Biochemistry, University of Washington, Seattle, WA, 98195-1700, USA
SOURCE: Bioorganic & Medicinal Chemistry (2001), 9(11), 2819-2825
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

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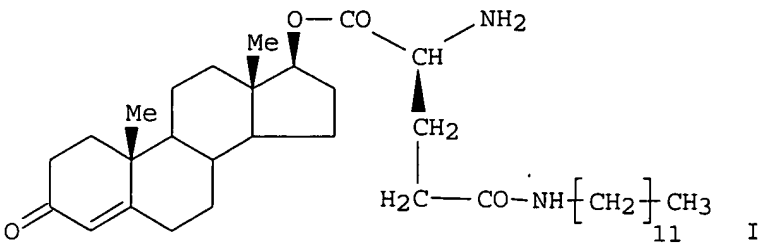

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AB Complex high axial ratio microstructures (CHARMssuch as I) were evaluated for delivery of **testosterone** in vivo. Methods to incorporate **testosterone** included noncovalent mixing and covalent attachment of **testosterone** to the lipid to form a **prodrug** monomer. When prepared by covalent attachment, **testosterone** -loaded CHARMs were resistant to in vitro spontaneous hydrolysis; when injected into rats, **testosterone** was released with biphasic kinetics consisting of a burst followed by a much slower phase. Some CHARM material associated with **testosterone** persisted at the site of injection for at least 9 days.

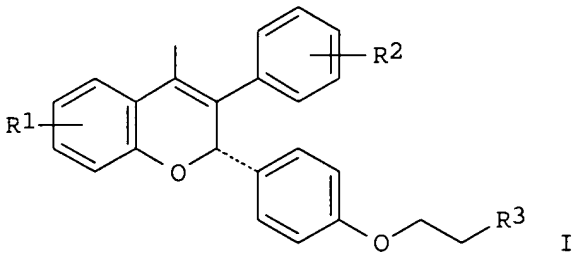
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 19 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:564841 HCAPLUS
DOCUMENT NUMBER: 135:132470
TITLE: Selective estrogen receptor modulators in combination with estrogens for therapeutic use
INVENTOR(S): Labrie, Fernand
PATENT ASSIGNEE(S): Endorecherche, Inc., Can.
SOURCE: PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001054699	A1	20010802	WO 2001-CA86	20010126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AA	20010802	CA 2001-2395730	20010126
	A1	20021030	EP 2001-902194	20010126
	, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, , FI, RO, MK, CY, AL, TR			
	A	20030311	BR 2001-8107	20010126
	T2	20030708	JP 2001-554683	20010126
	A1	20021226	US 2001-52803	20011107
	A1	20030227	US 2001-52824	20011107

US 2003065008	A1	20030403	US 2002-143894		20020509
NO 2002003484	A	20020722	NO 2002-3484		20020722
ZA 2002005926	A	20030724	ZA 2002-5926		20020724
PRIORITY APPLN. INFO.:			US 2000-178601P	P	20000128
			US 2001-771180	A1	20010126
			WO 2001-CA86	W	20010126

OTHER SOURCE(S): MARPAT 135:132470
GI



I

AB Methods for reduction or elimination of the incidence of hot flashes and menopausal symptoms, while decreasing the risk of acquiring breast or endometrial cancer and furthermore treating and/or inhibiting the development of osteoporosis, hypercholesterolemia, hyperlipidemia, atherosclerosis, hypertension, insulin resistance, diabetes, loss of muscle mass, obesity, irregular menstruation, Alzheimer's disease, or vaginal dryness in susceptible warm-blooded animals, including humans, involves administration of selective estrogen receptor modulators, particularly compds. I (R1, R2 = OH, moiety convertible to OH in vivo; R3 = (un)saturated (substituted) pyrrolidinyl, (un)saturated (substituted) piperidinyl, etc.) and an amount of an estrogen or mixed estrogenic/androgenic compound Further administration of bisphosphonates, or a sex steroid precursor is specifically disclosed for the medical treatment and/or inhibition of development of some of these above-mentioned diseases. Pharmaceutical compns. for delivery of active ingredient(s) and kit(s) useful to the invention are also disclosed.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 20 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:435015 HCAPLUS
DOCUMENT NUMBER: 135:33380
TITLE: Benzyl tetralins, formulations and uses thereof as inhibitors of 17β-hydroxy steroid dehydrogenase for treatment of androgen- and estrogen-mediated diseases
INVENTOR(S): Smith, Harold John; Mason, Peter; Ahmadi, Masoud; Nicholls, Paul Joseph; Greer, Valerie
PATENT ASSIGNEE(S): University College Cardiff Consultants Limited, UK
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001042181	A1	20010614	WO 2000-GB4700		20001208

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1999-29302 A 19991210

OTHER SOURCE(S): MARPAT 135:33380

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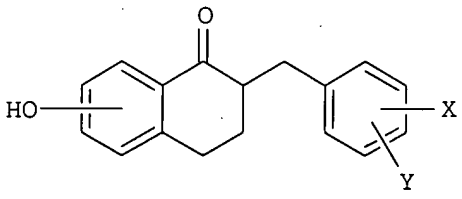

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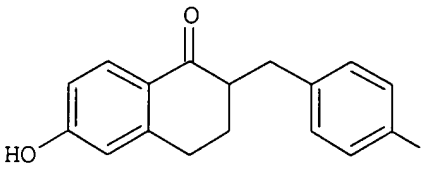

II

AB A benzyl tetralin I or a pharmaceutically acceptable salt or **prodrug** thereof is disclosed [wherein X = halogen, C1-6 alkyl (optionally substituted by at least one halogen), a fused bicyclic hydrophobic ring system, or Ph (optionally substituted by at least one halogen); Y = H or halogen; or X and Y together form the residue of a carbocyclic ring]. I are useful as inhibitors of 17β-hydroxy steroid dehydrogenase (17β-HSD) isoforms operable in the steroidogenesis pathway, and have therapeutic applications in the treatment of androgen- or estrogen-dependent or mediated diseases. In particular, I are useful for treating prostate cancer or breast cancer. I may be formulated with other steroidogenesis pathway enzyme inhibitors, where the inhibited enzyme is a 17β-HSD isoform, 5α-steroid reductase, aromatase P450arom, or estrogen sulfatase. Eight specific examples and their intermediates are described. For instance, 6-methoxy-3,4-dihydronaphthalen-1(2H)-one underwent a sequence of O-demethylation (57%), O-protection as the THP ether (86.8%), condensation with 4-chlorobenzaldehyde to give a 2-benzylidene derivative (51.7%), deprotection (94%), and hydrogenation of the benzylidene bond (69.5%), to give title compound II. This compound at 200 μM gave 97.9% inhibition of androstenedione reduction by human testicular microsomal 17β-HSD in vitro, and 59.6% inhibition of estrone reduction by human placental cytosolic 17β-HSD in vitro.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 16:42:20 ON 26 APR 2005)

FILE 'STNGUIDE' ENTERED AT 16:42:25 ON 26 APR 2005

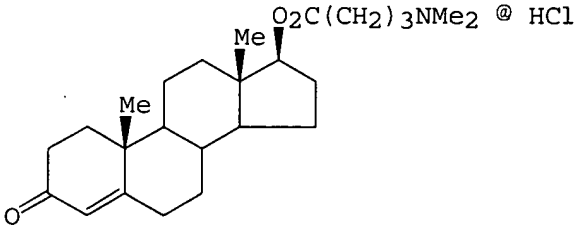
FILE 'HCAPLUS' ENTERED AT 16:42:37 ON 26 APR 2005
L1 57193 S TESTOSTERONE
L2 48 S L1 AND PRODRUG
L3 6 S L2 AND ETHER
L4 17 S L2 AND ESTER

=> d l2 35-48 ibib hitstr abs

L2 ANSWER 35 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:235356 HCAPLUS
DOCUMENT NUMBER: 120:235356
TITLE: Use of Caco-2 cells as an in vitro intestinal absorption and metabolism model
AUTHOR(S): Gan, Liang Shang; Eads, Cindy; Niederer, Tara; Bridgers, Avis; Yanni, Souzan; Hsyu, Poe Hirr; Pritchard, Fred J.; Thakker, Dhiren
CORPORATE SOURCE: Dep. Drug Metabolism, Glaxo Inc. Res. Inst., Research Triangle Park, NC, 27709, USA
SOURCE: Drug Development and Industrial Pharmacy (1994), 20(4), 615-31
CODEN: DDIPD8; ISSN: 0363-9045
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The Caco-2 cell line, a human colorectal carcinoma cell line, is an established in vitro model for the study of drug transport in the human intestine. The authors have routinely utilized this in vitro model to 1) elucidate intestinal absorption mechanisms of small drug mols. and peptide-like therapeutic agents (e.g. paracellular/transcellular passive diffusion and carrier-mediated active transport), 2) screen and select orally active therapeutic agents, 3) identify optimum luminal pH's for drug absorptions, 4) address dissoln. rate-related absorption problems, 5) assess mucosal toxicity of therapeutic agents, and 6) evaluate **prodrug** approaches for enhanced drug absorptions. The authors have also utilized this in vitro model to assess the metabolic stability of therapeutic agents in the intestinal epithelium. demonstrated in this report are primarily the techniques for the elucidation of absorption mechanisms. Examples of the characterization of paracellular/transcellular passive diffusion pathways and carrier-mediated active transport will be given. Application of the Caco-2 model to the process of drug development will also be discussed.

L2 ANSWER 36 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:197944 HCAPLUS
DOCUMENT NUMBER: 118:197944
TITLE: Testosteronyl 4-dimethylaminobutyrate·hydrochlo ride: a **prodrug** with improved skin penetration rate
AUTHOR(S): Milosovich, Susan; Hussain, Anwar; Dittert, Lewis; Aungst, Bruce; Hussain, Munir
CORPORATE SOURCE: SmithKline Beecham Pharm., King of Prussia, PA, 19406-0939, USA
SOURCE: Journal of Pharmaceutical Sciences (1993), 82(2),

227-8
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Testosteronyl 4-dimethylaminobutyrate-HCl (I) **prodrug** has a lipophilic portion and a tertiary amine group that exists in the protonated form at physiol. pH, making it more permeable through the skin. I penetration through the mice skin was 7-fold higher than that of the parent compound, **testosterone** (.apprx.140 and .apprx.20 ng/mL, resp.).

L2 ANSWER 37 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:455767 HCAPLUS
DOCUMENT NUMBER: 117:55767
TITLE: The in vitro enzymic labilities of chemically distinct phosphomonoester prodrugs
AUTHOR(S): Kearney, Albert S.; Stella, Valentino J.
CORPORATE SOURCE: Dep. Pharm. Chem., Univ. Kansas, Lawrence, KS, 66045, USA
SOURCE: Pharmaceutical Research (1992), 9(4), 497-503
CODEN: PHREEB; ISSN: 0724-8741
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The kinetics of decomposition of phosphomonoesters of hydroxymethyl-5,5-diphenylhydantoin (I), estrone (II), 17β- **testosterone** (III), 1-phenylvinyl alc. (IV), and 17α- **testosterone** (V) were studied in rat whole blood at 25 and(or) 37°. As the acidity of the leaving hydroxyl group of the phosphomonoester increased, there was a tendency for the rate of hydrolysis to increase, except for the anomalous behavior of IV, which was consistent with its relative rate of hydrolysis in aqueous solns. In addition, the kinetics of hydrolysis of I-V and p-nitrophenyl phosphate (p-NPP) were studied in the presence of isolated alkaline phosphatases from a variety of sources. The initial rate of production of 17α- and 17β- **testosterone** from their resp. phosphate esters, V and III, in the presence of human placental alkaline phosphatase, revealed that III was hydrolyzed 5.3-fold more rapidly than V. This difference in reactivity might have been the result of differences in the stereochem. and(or) steric nature of the 2 isomers. For p-NPP, I, II, and IV, the kcat and kcat/Km values determined in the presence of the various alkaline phosphatases showed little variation, whereas for III, the catalytic consts., kcat and kcat/Km, were dramatically less than those found for p-NPP, I, II, and IV. This suggested that the reaction steps, involving the noncovalent binding of the phosphomonoester

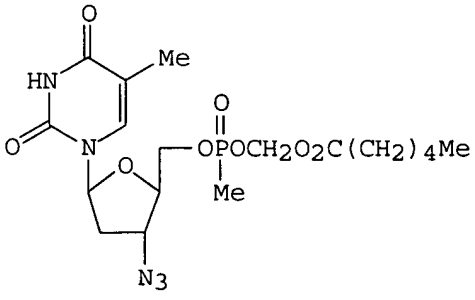
to the enzyme and(or) the nucleophilic displacement of the leaving alc. of the phosphomonoester by the reactive amino acid residue of the enzyme, might have been less favorable in the case of III, where the C atom of the ester linkage was secondary and was associated with a rigid ring system.

L2 ANSWER 38 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:449157 HCAPLUS
DOCUMENT NUMBER: 117:49157
TITLE: Preparation of brain-targeted acyloxymethylphosphonate prodrugs
INVENTOR(S): Bodor, Nicholas S.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 179 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9200988	A1	19920123	WO 1991-US4824	19910712
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MN, MW, NL, NO, PL, RO, SD, SE, SU				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
US 5177064	A	19930105	US 1990-553548	19900713
CA 2087194	AA	19920114	CA 1991-2087194	19910712
AU 9183000	A1	19920204	AU 1991-83000	19910712
AU 649466	B2	19940526		
EP 539493	A1	19930505	EP 1991-913701	19910712
EP 539493	B1	19970326		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05509313	T2	19931222	JP 1991-513064	19910712
AT 150759	E	19970415	AT 1991-913701	19910712
US 5413996	A	19950509	US 1992-962504	19921016
US 5618803	A	19970408	US 1994-340896	19941115

PRIORITY APPLN. INFO.: US 1990-553548 A 19900713
WO 1991-US4824 A 19910712
US 1992-962504 A3 19921016

OTHER SOURCE(S): MARPAT 117:49157
GI



II

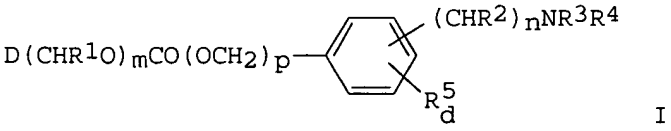
AB QP(O)(R1)OCHR2O2CR3 [Q = O-bonded drug moiety; R1 = alkyl, aryl, aralkyl; R2 = H, hetero)aryl, (cyclo)alkyl, heterocyclyl, aralkyl; R3 = alkyl,

alkenyl, (alkyl)cycloalkyl(alkyl), aryloxyalkyl, pyridyl, (substituted) Ph, phenylalkyl], were prepared Thus, zidovudine was stirred with MeP(O)Cl2 and Na2CO3 in acetone for 17 h; H2O was added to give 31.3% zidovudine methylphosphonate (I), which was treated with iodomethyl hexanoate and CsF in DMF to give title compound II. Title compds. are rapidly hydrolyzed in vivo, and I was found in the brain after administration of II.

L2 ANSWER 39 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:228552 HCAPLUS
DOCUMENT NUMBER: 114:228552
TITLE: Preparation of (aminoalkyl)phenylacyl-derivatized drugs with improved solution stability and solubility
INVENTOR(S): Bundgaard, Hans; Falch, Erik
PATENT ASSIGNEE(S): Den.
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9008128	A1	19900726	WO 1990-DK20		19900119
W: AU, CA, FI, JP, KR, NO, US					
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE					
CA 2045591	AA	19900721	CA 1990-2045591		19900119
AU 9050323	A1	19900813	AU 1990-50323		19900119
EP 454773	A1	19911106	EP 1990-902624		19900119
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE					
JP 04502918	T2	19920528	JP 1990-502553		19900119
PRIORITY APPLN. INFO.:			DK 1989-240	A	19890120
			WO 1990-DK20	A	19900119

OTHER SOURCE(S): MARPAT 114:228552
GI



I

AB The title compds. [I; D = residue of an NH- or OH-containing drug; R1 = H, alkyl, aryl, aralkyl, alkoxycarbonyl, carbamoyl; R2 = H, alkyl; R3, R4 = H, (substituted) alkyl, aralkyl, alkenyl, cycloalkyl; R3R4N = (substituted) heterocyclyl; R5 = halo, OH, alkyl, alkoxy; d = 0-4; m,p = 0,1; n = 1-4] were prepared as prodrugs having improved stability in aqueous solution Thus, hydrocortisone in CH2Cl2 was stirred with Et3N and 3-ClCH2C6H4COCl to give hydrocortisone 21-(3-chloromethyl)benzoate. The latter was stirred with NaI and N-methylpiperazine in Me2CO at 60° to give hydrocortisone 21-[3-(4-methylpiperazin-1-yl)methyl]benzoate, converted to the dihydrochloride. The latter had solubility of 3.5 mg/mL in H2O at 21°, vs. 0.40 mg/mL for hydrocortisone itself. I are preferably stored at pH 3-5. I derivs. of hydrocortisone showed t1/2 of

8-147 min in human plasma at pH 7.4.

L2 ANSWER 40 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:88647 HCAPLUS
DOCUMENT NUMBER: 114:88647
TITLE: Preparation of cyclodextrin derivatives for active agent delivery as inclusion complexes and for separating racemic mixtures
INVENTOR(S): Lincoln, Stephen Frederick; Coates, John Hewlett; Easton, Christopher John; Van Eyk, Stephen John; May, Bruce Lindly; Singh, Paramjit; Williams, Michael Lloyd; Stile, Martyn Allen
PATENT ASSIGNEE(S): Australian Commercial Research and Development Ltd., Australia
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9002141	A1	19900308	WO 1989-AU359	19890823
W: AU, BB, BG, BR, DK, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, FR, GA, GB, IT, LU, ML, MR, NL, SE, SN, TD, TG				
AU 8944290	A1	19900323	AU 1989-44290	19890823
AU 693072	B2	19980625		
EP 431080	A1	19910612	EP 1989-911240	19890823
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
BR 8907625	A	19910820	BR 1989-7625	19890823
JP 04500229	T2	19920116	JP 1989-510576	19890823
CN 1040987	A	19900404	CN 1989-106650	19890830
DD 297833	A5	19920123	DD 1989-332260	19890831
ZA 8906624	A	19920129	ZA 1989-6624	19900830
US 5324750	A	19940628	US 1992-979451	19921120

PRIORITY APPLN. INFO.:		
AU 1988-165	A	19880831
AU 1988-189	A	19880901
AU 1988-618	A	19880927
AU 1988-1053	A	19881019
AU 1988-1198	A	19881027
AU 1988-1417	A	19881111
AU 1989-4894	A	19890626
AU 1989-4909	A	19890626
AU 1989-5034	A	19890703
AU 1989-5278	A	19890717
AU 1989-5354	A	19890719
AU 1989-5576	A	19890803
AU 1989-5641	A	19890807
AU 1989-5682	A	19890809
WO 1989-AU359	A	19890823
US 1991-684888	B1	19910412

AB Cyclodextrin derivs. are prepared, which form soluble and stable inclusion complexes and covalently-bonded compds. with drugs, pesticides and cosmetics. The cyclodextrin derivs. have ≥1 NH2 group substituted with OH at C-2, C-3, or C-6. 6A-O-p-Toluenesulfonyl-β-cyclodextrin prepared as usual, was treated with Na azide and 1,1,2,2-tetrachloroethane,

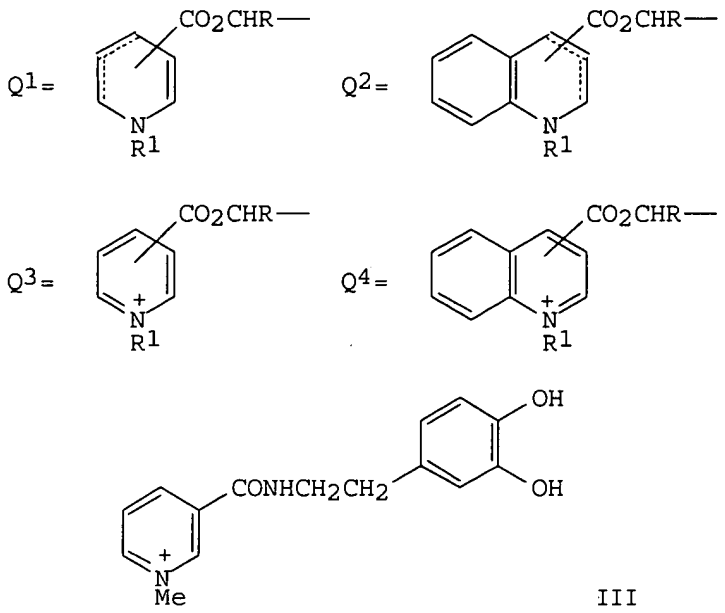
to give 6A-azido-6A-deoxy-β-cyclodextrin, which was hydrogenated over Pd black, in water, to yield 6A-amino-6A-deoxy-β-cyclodextrin. This was treated with ibuprofen anhydride to give 6A-deoxy-6A-(α-methyl-4-isobutylphenylacetamido)-β-cyclodextrin, a **prodrug** for ibuprofen delivery. The cyclodextrin derivs. and their inclusion complexes may also be used for the chromatog. separation of enantiomers from racemic mixts.

L2 ANSWER 41 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:104779 HCAPLUS
DOCUMENT NUMBER: 112:104779
TITLE: The utilization of prodrugs to enhance transdermal penetration of **testosterone**, deoxycorticosterone, and indomethacin
AUTHOR(S): Milosovich, Susan Marie
CORPORATE SOURCE: Univ. Kentucky, Lexington, KY, USA
SOURCE: (1988) 191 pp. Avail.: Univ. Microfilms Int., Order No. DA8914912
From: Diss. Abstr. Int. B 1989, 50(4), 1428
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L2 ANSWER 42 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:7383 HCAPLUS
DOCUMENT NUMBER: 112:7383
TITLE: Preparation of dihydropyridine-containing prodrugs for brain-specific drug delivery
INVENTOR(S): Bodor, Nicholas S.
PATENT ASSIGNEE(S): University of Florida, USA
SOURCE: U.S., 282 pp. Cont.-in-part of U.S. 4,479,932.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4824850	A	19890425	US 1984-665940	19841029
US 4479932	A	19841030	US 1982-379316	19820518
US 4622218	A	19861111	US 1983-475493	19830315
EP 218300	A2	19870415	EP 1986-201710	19830512
EP 218300	A3	19880928		
R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE				
EP 221588	A2	19870513	EP 1986-201711	19830512
EP 221588	A3	19880921		
R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE				
EP 222425	A2	19870520	EP 1986-201714	19830512
EP 222425	A3	19880921		
R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE				
EP 224283	A2	19870603	EP 1986-201713	19830512
EP 224283	A3	19880921		
R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE				
EP 256577	A2	19880224	EP 1987-201385	19830512
EP 256577	A3	19880706		
R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE				
EP 262696	A2	19880406	EP 1987-201384	19830512
EP 262696	A3	19880720		

R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE					
CA 1253856	A1	19890509	CA 1983-428192		19830516
ZA 8303521	A	19841224	ZA 1983-3521		19830517
US 4540564	A	19850910	US 1983-516382		19830722
US 4727079	A	19880223	US 1985-733463		19850513
US 4880921	A	19891114	US 1987-75830		19870720
US 4900837	A	19900213	US 1987-76191		19870721
EP 334853	A1	19891004	EP 1987-907186		19871013
EP 334853	B1	19930609			
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
AT 90355	E	19930615	AT 1987-907186		19871013
US 4880816	A	19891114	US 1987-116583		19871104
US 5008257	A	19910416	US 1989-295938		19890111
US 5187158	A	19930216	US 1991-639283		19910110
US 5525727	A	19960611	US 1992-967979		19921028
PRIORITY APPLN. INFO.:			US 1982-379316	A2	19820518
			US 1983-461543	A2	19830127
			US 1983-475493	A2	19830315
			CA 1983-428192	A	19830516
			US 1983-516382	A2	19830722
			JP 1982-101940	A	19820614
			EP 1983-902034	P	19830512
			WO 1983-US725	A	19830512
			WO 1983-WO725	A	19830512
			ES 1983-522489	A	19830517
			IE 1983-1149	A	19830517
			ZA 1983-3521	A	19830517
			IT 1983-48327	A	19830518
			US 1984-665940	A2	19841029
			US 1985-733463	A3	19850513
			EP 1987-907186	A	19871013
			WO 1987-US2590	A	19871013
			US 1989-295938	A3	19890111
			US 1991-639283	A3	19910110
OTHER SOURCE(S):	CASREACT 112:7383; MARPAT 112:7383				
GI					



III

AB Compds. of the formula D(DHC)n (I) [D = residue of a centrally acting drug having anticonvulsant, sedative and/or hypnotic properties, said drug being a hydantoin or barbiturate or an analog of a hydantoin or barbiturate, said drug containing at least one reactive amide or imide functional group, said residue being characterized by the absence of a H atom from at least one of said amide or imide functional groups in said drug; n = pos. integer equal to the number of said functional groups from which a H atom is absent; DHC = reduced, biooxidizable, blood-brain barrier penetrating, lipoidal form of a dihydropyridine-pyridinium salt redox carrier; DHC = Q1, Q2, etc.; R = H, C1-7 alkyl, C3-8 cycloalkyl, C1-7 haloalkyl, etc.; R1 = C1-7 alkyl, haloalkyl, C7-10 aralkyl; dotted line indicates the presence of a double bond in position 4 or 5 of the dihydropyridine ring or position 2 or 3 of the dihydroquinoline ring] were prepared as brain-specific prodrugs. Quaternary salts of the formula D(QC+)nqX-t (II) (D = as given above; X- = anion of a pharmaceutically acceptable organic or inorg. acid; t = valence of acid anion; q = number which when multiplied by t is equal to n; QC+ = hydrophilic, ionic pyridinium salt form of a dihydropyridine-pyridinium salt redox carrier; QC+ = Q3, Q4, etc.; R, R1 = as given above; n = pos. integer equal to the number of said functional groups from which a H atom is absent) were prepared as intermediates for I. Reaction of 5,5-diphenyl-3-hydroxymethyl-2,4-imidazolidinedione with nicotinic anhydride, followed by methylation with MeI and reduction, gave 5,5-diphenyl-3-[(1'-methyl-1',4'-dihydropyridin-3'-yl)carbonyloxymethyl]-2,4-imidazolidinedione. After one single injection of 1-methyl-3-[[N-[β-(3,4-dipivalyloxyphenyl)ethyl]]carbamoyl-1,4-dihydropyridine to a rat, the pyridinium compound III could be seen to appear and then to disappear quickly from the blood, with a half-life of 27 min. On the contrary, the concentration of III increases in the brain steadily, reaching a maximum at about 30 min following administration. For III, the half-life of diappearance from the brain is about 3.2 h.

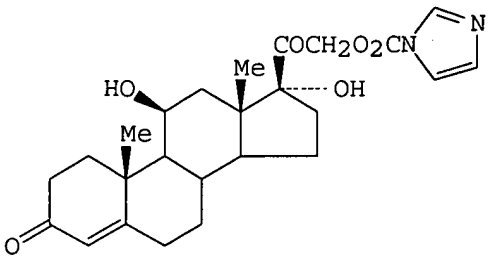
L2 ANSWER 43 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:428472 HCAPLUS
DOCUMENT NUMBER: 111:28472

09872705

TITLE: The utilization of prodrugs to enhance transdermal absorption of **testosterone**, deoxycorticosterone and indomethacin
AUTHOR(S): Milosovich, S. M.; Hussain, Anwar A.; Hussain, M.; Dittert, Lewis W.
CORPORATE SOURCE: Coll. Pharm., Univ. Kentucky, Lexington, KY, 40536, USA
SOURCE: Progress in Clinical and Biological Research (1989), 292(Biol. Synth. Membr.), 273-7
CODEN: PCBRD2; ISSN: 0361-7742
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ester prodrugs which contain a protonated tertiary amine at physiol. pH were used successfully to enhance the skin penetration of indomethacin, deoxycorticosterone, and **testosterone.** The prodrugs are enzymically hydrolyzed to their active parent compds. in the body, and therefore are expected to elicit the desired pharmacol. response.

L2 ANSWER 44 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:428418 HCAPLUS
DOCUMENT NUMBER: 111:28418
TITLE: Studies on long-acting aryl carboxylic acid esters of **testosterone**
AUTHOR(S): Leung, S. L.; Becket, G.; Karunanithy, R.; Low, K. F.; Fell, J. T.
CORPORATE SOURCE: Dep. Pharm., Natl. Univ. Singapore, Singapore, 0511, Singapore
SOURCE: Pharmaceutica Acta Helvetiae (1989), 64(4), 121-4
CODEN: PAHEAA; ISSN: 0031-6865
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of aryl carboxylic acid esters of **testosterone** were synthesized as possible agents for long-acting steroid therapy. The solubilities, partition coeffs., and hydrolysis rate consts. of the compds. were determined The partition coeffs. increased with increasing chain length and they were in agreement with calculated values. The hydrolysis rates decreased with increasing chain length except for the first member of the series (benzoate ester) which exhibits the slowest rate, possibly due to the hydrolytic attack being hindered by steric and electronic effects.

L2 ANSWER 45 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:67298 HCAPLUS
DOCUMENT NUMBER: 102:67298
TITLE: Prodrugs as drug delivery systems. XXIX. Imidazole-1-carboxylic acid esters of hydrocortisone and **testosterone**
AUTHOR(S): Klixbull, Ulla; Bundgaard, Hans
CORPORATE SOURCE: Dep. Pharm. Chem., R. Dan. Sch. Pharm., Copenhagen, DK-2100, Den.
SOURCE: Archiv for Pharmaci og Chemi, Scientific Edition (1983), 11(4), 1065-74
CODEN: AVPCCS; ISSN: 0302-248X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The kinetics of hydrolysis of hydrocortisone imidazole-1-carboxylic acid ester (I) [51988-89-7] and **testosterone** imidazole-1-carboxylic acid ester [51242-05-8] was studied to assess their suitability as **prodrug** forms. The pH-rate profiles of the 2 derivs. were derived in the range pH 1-12 and were accounted for by assuming spontaneous hydrolysis of the protonated forms (pKa 3.3-3.5) and OH--catalyzed hydrolysis of the free base forms. At pH 7.4 and 37° the half-life of hydrolysis of I was 8 min and that for the **testosterone** derivative 65 h. These rates were not significantly altered in the presence of human plasma. Due to protonation of the imidazole group, the derivs. showed increased solubility in acidic aqueous solution, the enhancement amounting to a factor of 16 for the **testosterone** derivative

L2 ANSWER 46 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:91670 HCAPLUS
DOCUMENT NUMBER: 96:91670
TITLE: Prolonged action drug formulation
INVENTOR(S): Swarbrick, James
PATENT ASSIGNEE(S): University of California, Los Angeles, USA
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 8102975	A1	19811029	WO 1981-US520		19810420
W: AU, DK, JP					
RW: CH, DE, FR, GB, NL, SE					
AU 8172201	A1	19811110	AU 1981-72201		19810420
EP 50650	A1	19820505	EP 1981-901250		19810420
R: CH, DE, FR, GB, NL, SE					
CA 1168581	A1	19840605	CA 1981-375991		19810422
PRIORITY APPLN. INFO.:			US 1980-142279	A	19800421
			WO 1981-US520	A	19810420

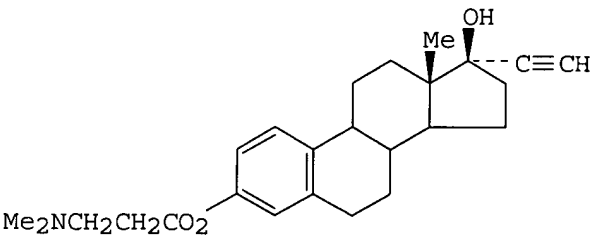
AB A prolonged-action drug formulation comprises a drug in solid form and a solid chemical derivative of the drug in a concentration sufficient to prolong the time during which the drug is active and having, at said concentration, minor pharmacol. activity relative to the drug. Thus, dapsone [80-08-0] and acedapsone [77-46-3] each at 0.5 g can be admixed, the mixture suspended in 3 mL H2O for injection and administered to a person suffering from leprosy as an i.m. injection of 3 mL (containing 1 g of the combination), the

injection being repeated only once/mo instead of the typical dosage of 50-100 mg/day for 5 yr or more.

L2 ANSWER 47 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:69405 HCAPLUS
DOCUMENT NUMBER: 96:69405
TITLE: Synthesis of polymers with pharmacological properties. Introduction of peptide sequences into the macromolecular chain
AUTHOR(S): Pleurdeau, A.; Rabadeux, J. C.; Gueniffey, H.; Lenuz, C.
CORPORATE SOURCE: Fac. Sci., Univ. Maine, Le Mans, 72017, Fr.
SOURCE: European Polymer Journal (1981), 17(9), 999-1003
CODEN: EUPJAG; ISSN: 0014-3057
DOCUMENT TYPE: Journal
LANGUAGE: French

AB Polypeptides were prepared from N-carboxyanhydrides bearing active steroidal groups. Introduction of peptide sequences into polymers with pharmacol. properties increased the biocompatibility of the macromol. **prodrug**. Lysine Cu complex reacted with the chloroformates of cholesterol and **testosterone** to give Cu complexes of H-Lys(CO2R)-OH (R = cholesteryl, testosteryl). The latter Cu complexes were deblocking and cyclized with COCl2 to give the corresponding N-carboxyanhydrides. The polymerization of these carboxyanhydrides alone and with glycine N-carboxyanhydride gave oligopeptides bearing a steroidal backbone as a side group. The low mol. weight of the synthesized compds., the limited H2O solubility and the presence of secondary products limited the development of the method.

L2 ANSWER 48 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:500578 HCAPLUS
DOCUMENT NUMBER: 89:100578
TITLE: Steroid antifertility agents. Ionic complexes of basic derivatives for prolonged action
AUTHOR(S): Gray, Allan P.; Yamauchi, Terry N.
CORPORATE SOURCE: Chem. Chem. Eng. Res. Div., Res. Inst., Chicago, IL, USA
SOURCE: Journal of Medicinal Chemistry (1978), 21(7), 712-15
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Ethynylestradiol 3-dimethylaminopropionate (I) [60257-22-9], sym- [66818-36-8] and anti-norethindrone 3-(O-dimethylaminopropyl)oxime [66818-34-6], and **testosterone** 3-(O-dimethylaminopropyl)oxime [66818-35-7] were prepared and converted to Zn and Al tannate complexes and

were tested as potential long-acting **prodrug** forms of the parent steroids. The Zn tannate complex of I administered s.c. in an Al monosterate gel, had a prolonged duration of antifertility activity in rats. All of the basic derivs. and complexes had appropriate hormonal activities but in acute tests were less active than the resp. parents.

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(FILE 'HOME' ENTERED AT 16:42:20 ON 26 APR 2005)

FILE 'STNGUIDE' ENTERED AT 16:42:25 ON 26 APR 2005

FILE 'HCAPLUS' ENTERED AT 16:42:37 ON 26 APR 2005
L1 57193 S TESTOSTERONE
L2 48 S L1 AND PRODRUG
L3 6 S L2 AND ETHER
L4 17 S L2 AND ESTER

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L2 ANSWER 21 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:392436 HCAPLUS
DOCUMENT NUMBER: 135:204880
TITLE: A novel cytochrome P450 enzyme responsible for the metabolism of ebastine in monkey small intestine
AUTHOR(S): Hashizume, Takanori; Mise, Masashi; Matsumoto, Satoshi; Terauchi, Yoshiaki; Fujii, Toshihiko; Imaoka, Susumu; Funae, Yoshihiko; Kamataki, Tetsuya; Miyazaki, Hisashi
CORPORATE SOURCE: Developmental Research Laboratories, Dainippon Pharmaceutical Co., Ltd., Osaka, 564-0053, Japan
SOURCE: Drug Metabolism and Disposition (2001), 29(6), 798-805
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Small intestinal microsomes of cynomolgus monkeys were found to catalyze hydroxylation and dealkylation of an H1-antihistamine **prodrug**, ebastine. To identify the main enzyme responsible for ebastine hydroxylation, which has been hitherto unknown, we purified two cytochrome P 450 isoforms, named P 450 MI-2 and P 450 MI-3, from the intestinal microsomes on the basis of the hydroxylation activity. P 450 MI-2 and P 450 MI-3 showed the resp. apparent mol. wts. of 56,000 and 53,000 on sodium dodecyl sulfate-polyacrylamide gel electrophoresis. The internal amino acid sequence of P 450 MI-2 had high similarity with those of human CYP4F2, CYP4F3, and CYP4F8. The first 27 amino acid residues of P 450 MI-3 were highly homologous with those of monkey CYP3A8 and human CYP3A4/5/7. Furthermore, P 450 MI-2 and P 450 MI-3 were recognized by anti-CYP4F and anti-CYP3A antibodies, resp., in immunoblot anal. and catalyzed leukotriene B4 ω-hydroxylation and **testosterone** 6β-hydroxylation, which are known to be mediated by CYP4F and CYP3A, resp. Although both enzymes had ebastine hydroxylation activity, the Vmax value of P 450 MI-2 was much higher than that of P 450 MI-3 (37.0 vs. 0.406 nmol/min/nmol of P 450), and the former KM (5.1 μM) was smaller than the latter KM (10 μM). Anti-CYP4F antibody inhibited the hydroxylation in small intestinal microsomes strongly (70%), but anti-CYP3A antibody did not. These results indicate that P 450 MI-2

belongs to the CYP4F subfamily and is mainly responsible for hydroxylation of ebastine in monkey small intestinal microsomes. This suggests that the small intestinal CYP4F enzyme, P 450 MI-2, can play an important role in the metabolism of drugs given orally.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 22 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:592532 HCAPLUS
DOCUMENT NUMBER: 133:183007
TITLE: Preparation of phosphocholine linked **prodrug** derivatives
INVENTOR(S): Morimoto, Bruce H.; Barker, Peter L.
PATENT ASSIGNEE(S): Amur Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000048572	A1	20000824	WO 2000-US4140	20000216
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1161226	A1	20011212	EP 2000-908713	20000216
EP 1161226	B1	20040526		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002537243	T2	20021105	JP 2000-599364	20000216
AT 267586	E	20040615	AT 2000-908713	20000216
PRIORITY APPLN. INFO.:			US 1999-120483P	P 19990218
			WO 2000-US4140	W 20000216

OTHER SOURCE(S): MARPAT 133:183007
AB Prodrugs containing phosphocholines enhance the bioavailability of the linked drugs wherein the linker is (i) substituted or unsubstituted alkyl, (ii) substituted or unsubstituted alkenyl, (iii) substituted or unsubstituted alkanoyl, (iv) substituted or unsubstituted alkenoyl and wherein the therapeutic agent is an alc.-containing water-insol. steroid. A phosphocholine-linked propofol [{2',6'-diisopropylphenyl 4-(2-trimethylammoniumethoxy)phosphonobutyrate}] was prepared starting from trans-Et 4-hydroxycrotonate and through a sequence of reactions involving propofol and 2-chloro-2-oxo-1,3,2-dioxaphospholane. The **prodrug** was tested for its sedative activity.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 23 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:547377 HCAPLUS
DOCUMENT NUMBER: 133:155440
TITLE: In situ activation of microcapsules

INVENTOR(S): Morrison, Dennis R.; Mosier, Benjamin
PATENT ASSIGNEE(S): United States National Aeronautics and Space Administration, USA
SOURCE: U.S., 28 pp., Cont.-in-part of U.S. 5,827,531.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6099864	A	20000808	US 1998-79741	19980515
US 349169	A0	19971007	US 1994-349169	19941202
US 5827531	A	19981027		
WO 9959554	A1	19991125	WO 1999-US10653	19990514
W: JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.: US 1994-349169 A2 19941202
US 1998-79741 A 19980515

AB Disclosed are microcapsules comprising a polymer shell enclosing two or more immiscible liquid phases in which a drug, or a **prodrug** and a drug activator are partitioned into sep. phases, or prevented from diffusing out of the microcapsule by a liquid phase in which the drug is poorly soluble Also disclosed are methods of using the microcapsules for in situ activation of drugs, where upon exposure to an appropriate energy source the internal phases mix and the drug is activated in situ. An example of a microcapsule, suitable for in situ activation of a **prodrug** is shown schematically. In this embodiment the **prodrug**, floxuridine, may be contained in the continuous, internal aqueous phase. The activator, thymidine kinase is also contained within the microcapsule. During irradiation with UV light of 300-390 nm, the internal liquid phases in the microcapsules exhibit a spontaneous, vigorous mixing action with brings the contents of the two phases together, and increases the activation kinetics of the water soluble floxuridine to the water insol. active form 5-FU, which diffuses out of the microcapsule.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 24 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:753042 HCAPLUS
DOCUMENT NUMBER: 131:356128
TITLE: In situ activation of microcapsules
INVENTOR(S): Morrison, Dennis R.; Mosier, Benjamin
PATENT ASSIGNEE(S): NASA/Johnson Space Center, USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9959554	A1	19991125	WO 1999-US10653	19990514
W: JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

US 6099864 A 20000808 US 1998-79741 19980515
PRIORITY APPLN. INFO.: US 1998-79741 A 19980515
US 1994-349169 A2 19941202

AB Disclosed are microcapsules comprising a polymer shell enclosing two or more immiscible liquid phases in which a drug, or a **prodrug** and a drug activator are partitioned into sep. phases, or prevented from diffusing out of the microcapsule by a liquid phase in which the drug is poorly soluble Also disclosed are methods of using the microcapsules for in situ activation of drugs, where upon exposure to an appropriate energy source the internal phases mix and the drug is activated in situ. The **prodrug**, floxuridine may be contained in a continuous, internal aqueous phase. The activator, thymidine kinase is also contained within the microcapsule. During irradiation with UV light of 300-390 nm, the internal liquid phases in the microcapsules had a spontaneous, vigorous mixing action which brings the contents of the 2 phases together, and increases the activation kinetics of the water soluble floxuridine to the water-insol. active form 5-FU, which diffuses out of the microcapsule.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 25 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:557633 HCAPLUS
DOCUMENT NUMBER: 127:239118
TITLE: Drug delivery systems containing ester sunscreens and penetration enhancers
INVENTOR(S): Reed, Barry Leonard; Morgan, Timothy Matthias; Finnin, Barrie Charles
PATENT ASSIGNEE(S): Monash University, Australia; Reed, Barry Leonard; Morgan, Timothy Matthias; Finnin, Barrie Charles
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9729735	A1	19970821	WO 1997-AU91	19970219
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2244089	AA	19970821	CA 1997-2244089	19970219
AU 9717134	A1	19970902	AU 1997-17134	19970219
AU 706967	B2	19990701		
EP 901368	A1	19990317	EP 1997-904304	19970219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000504697	T2	20000418	JP 1997-528834	19970219
US 6299900	B1	20011009	US 1998-125436	19981218
AU 9952589	A1	19991202	AU 1999-52589	19991001
US 2002028235	A1	20020307	US 2001-910780	20010724
US 6818226	B2	20041116		
US 2004013620	A1	20040122	US 2003-428016	20030502

US 2004013621	A1	20040122	US 2003-428019	20030502
US 2004028625	A1	20040212	US 2003-428012	20030502
US 2004028725	A1	20040212	US 2003-428018	20030502
US 2004096405	A1	20040520	US 2003-636976	20030808
US 2004081684	A1	20040429	US 2003-644085	20030820
US 2004146469	A1	20040729	US 2004-759303	20040120
PRIORITY APPLN. INFO.:			AU 1996-8144	A 19960219
			AU 1997-17134	A3 19970219
			WO 1997-AU91	W 19970219
			US 1998-125436	A3 19981218
			US 2001-910780	A2 20010724

OTHER SOURCE(S): MARPAT 127:239118

AB A transdermal drug delivery system which comprises at least one physiol. active agent or **prodrug** thereof and at least one dermal penetration enhancer; characterized in that the dermal penetration enhancer is a safe skin-tolerant ester sunscreen. A non-occlusive, percutaneous or transdermal drug delivery system which comprises: (1) an effective amount of at least one physiol. active agent or **prodrug** thereof; (2) at least one non-volatile dermal penetration enhancer; and (3) at least one volatile liquid; characterized in that the dermal penetration enhancer is adapted to transport the physiol. active agent across a dermal surface or mucosal membrane of an animal, including a human, when the volatile liquid evaps., to form a reservoir or depot of a mixture comprising the penetration enhancer and the physiol. active agent or **prodrug** within said surface or membrane; and the dermal penetration enhancer is of low toxicity to, and is tolerated by, the dermal surface or mucosal membrane of the animal. The mean flux of 2% ketoprofen in 70% volume/volume aqueous ethanol through shed snakes kinetics in presence of 2% octyl salicylate in 70% volume/volume aqueous ethanol was 27.66 as
compared to 2.58 μg/cm2.h for azone. A transdermal aerosol contained 17β-estradiol 2, octyl dimethyl-p-aminobenzoate 8, ethanol 69, and di-Me ether 30%.

L2 ANSWER 26 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1997:335797 HCAPLUS
DOCUMENT NUMBER:	127:44396
TITLE:	Enhanced cyclophosphamide and ifosfamide activation in primary human hepatocyte cultures: response to cytochrome P-450 inducers and autoinduction by oxazaphosphorines
AUTHOR(S):	Chang, Thomas K. H.; Yu, Li; Maurel, Patrick; Waxman, David J.
CORPORATE SOURCE:	Division Cell Moleuclar Biology, Department Biology, Boston University, Boston, MA, 02215, USA
SOURCE:	Cancer Research (1997), 57(10), 1946-1954 CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER:	American Association for Cancer Research
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The anticancer oxazaphosphorine prodrugs cyclophosphamdie and ifosfamide are activated in human liver by a 4-hydroxylation reaction catalyzed by multiple cytochrome P 450 (CYP) enzymes. In the present study, we used a cultured human hepatocyte model to identify possible inducers of the CYP-catalyzed activation fo these two anticancer prodrugs. Treatment of primary cultures of human hepatocytes with phenobarbital, dexamethasone, or rifampin elevated hepatocyte microsomal oxazaphosphorine 4-hdyroxylation by up to 200-400% of control for both drug substrates. These inductions were associated with corresponding increases in

immunoreactive CYP2B6, CYP2C8, CYP2C9, and CYP3A4, all previously shown to catalyze oxazaphosphorine activation. Rifampin (1 μM, 96-h exposure) was a particularly potent inducer of ifosfamide and cyclophosphamide 4-hydroxylation, as well as of CYP3A protein levels and CYP3A-dependent **testosterone** 6β-hydroxylation. CYP3A4, CYP2C8, and CYP2C9 protein levels were also increased by exposure of the hepatocytes to cyclophosphamide or ifosfamide (50 μM), which thereby enhanced their own rats of 4-hydroxylation in the cultured hepatocytes. IN one human hepatocyte culture that contained the polymorphically expressed CYP3A5 in addition to the more widely expressed CYP3A4, only CYP3A4 was induced by cyclophosphoamide, ifosfamide, and rifampin. These studies: (a) demonstrate an underlying metabolic basis for the clin. important oxazaphosphorine autoinduction pharmacokinetics seen with these drugs in cancer patients; and (b) identify rifampin and other CYP inducers as potentially useful for increasing the rates of cyclophosphamide 4-hydroxylation and ifosfamide 4-hydroxylation in human liver in a manner that could favorably impact the clin. pharmacokinetics of these anticancer prodrugs.

REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 27 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:287176 HCAPLUS
DOCUMENT NUMBER: 126:347281
TITLE: **Testosterone** prodrugs for improved drug delivery
INVENTOR(S): Hale, Ron L.; Lu, Amy T.; Solas, Dennis W.; Cormier, Michel J. N.
PATENT ASSIGNEE(S): Affymax Technologies N.V., UK; Alza Corporation
SOURCE: U.S., 30 pp., Cont.-in-part of U.S. Ser. No. 898,219, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 5622944	A	19970422	US 1995-434892		19950504
US 5607691	A	19970304	US 1995-449188		19950524
PRIORITY APPLN. INFO.:			US 1992-898219	B2	19920612
			US 1993-9463	B2	19930127
			US 1993-77296	B2	19930614
			US 1993-164293	B1	19931209

OTHER SOURCE(S): MARPAT 126:347281

AB Compns. and methods are provided for enhanced transdermal electrotransport of 17-hydroxy sterol compds., including **testosterone.** The parent sterols are modified at the 17-hydroxy position by covalent attachment of a charged chemical modifier. The chemical modifier provides the parent sterol with enhanced transport properties and is hydrolyzed under physiol. conditions to release the active parent compound The composition comprises a 17-hydroxy sterol/chemical modifier complex, more generally represented by the formula (sterol-O-)C(O)-R-N(R1)(R2)(R3)+. The portion of the complex derived from the chemical modifier is indicated by C(O)-R-N(R1)(R2)(R3)+, where N(R1)(R2)(R3)+ represents a quaternary ammonium group and R1, R2, and R3 are independently selected from the group consisting of lower alkyl, alkyl, aryl, arylalkyl, cycloalkyl, heteroalkyl, and heteroarylalkyl; or R1 and R2 together with the nitrogen

to which they are attached form a substituted heterocycle and R3 is lower alkyl, and R is a linking moiety, linking the (sterol-O)-C(O)- to the nitrogen atom.

L2 ANSWER 28 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:281690 HCAPLUS
DOCUMENT NUMBER: 126:338338
TITLE: Inhibition by omeprazole of proguanil metabolism: mechanism of the interaction in vitro and prediction of in vivo results from the in vitro experiments
AUTHOR(S): Funck-Brentano, Christian; Becquemont, Laurent; Leneveu, Anne; Roux, Annie; Jaillon, Patrice; Beaune, Philippe
CORPORATE SOURCE: Clinical Pharmacology Unit, Saint-Antoine University Hospital-School of Medicine, Paris, Fr.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1997), 280(2), 730-738
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Both the antimalarial **prodrug** proguanil and the gastric proton pump inhibitor omeprazole are substrates for cytochrome P 450 (CYP)2C19 and CYP3A. However, the relative contribution of each enzyme to proguanil bioactivation to cycloguanil and to the metabolism of omeprazole, as well as their potential to interact, remains to be examined The bioactivation of proguanil to its active metabolite cycloguanil was studied in vitro in human liver microsomes and in vivo in 12 healthy subjects, in the absence and in the presence of omeprazole. The formation of cycloguanil from proguanil exhibited biphasic kinetic behavior in four of six human livers, indicating that at least two enzymes are responsible for this metabolic step. Cycloguanil formation activity did not correlate with immunoreactive CYP3A4 content or with CYP3A4 activity, as measured by **testosterone** 6β-hydroxylation, suggesting that CYP3A4 plays a limited role in cycloguanil formation. Furthermore, troleandomycin (10 μM) inhibited only 10 to 17% of cycloguanil formation at proguanil concns. of 100 and 500 μM. At a proguanil concentration of 20 μM, omeprazole at 10 μM inhibited cycloguanil formation in vitro by 47 ± 59%. These in vitro results were consistent with the results of our in vivo study in healthy subjects, which showed a 32 ± 11% decrease in proguanil apparent oral clearance and a 65 ± 8% decrease in proguanil partial metabolic clearance to cycloguanil in the presence of omeprazole (both $P < .001$). We conclude that in vitro studies of proguanil metabolism and interactions are predictive of in vivo situations, that CYP2C19 is the main enzyme responsible for proguanil bioactivation to cycloguanil and that omeprazole inhibits this biotransformation in vitro and in vivo by inhibiting this enzyme.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 29 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:310727 HCAPLUS
DOCUMENT NUMBER: 125:18815
TITLE: Metabolism of **testosterone** and its ester derivatives in organotypic coculture of human dermal fibroblasts with differentiated epidermis
AUTHOR(S): Tamura, Mihoko; Sueishi, Toshihiko; Sugibayashi, Kenji; Morimoto, Yasunori; Juni, Kazuhiko; Hasegawa, Tetsuya; Kawaguchi, Takeo

CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Josai University, 1-1 Keyakidai, Sakado, Saitama, 35002, Japan
SOURCE: International Journal of Pharmaceutics (1996), 131(2), 263-271
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The metabolism of **testosterone** (TS) and its 17-O-acyl derivs. (acyl = acetyl, benzoyl and hemisuccinoyl) was studied using radioactive compds. in organotypic coculture of human dermal fibroblasts (living skin equivalent, LSE). When TS was applied to the epidermal-side of LSE in a small volume of acetone solution, both 5α-reduced and 17-dehydrogenated metabolites were observed in the dermal-side culture solution, though the formation of the 5α-reduced metabolites, dihydrotestosterone (DHT) and dihydroandrosterone (DHA), depended greatly on the culture conditions. The metabolic activity of LSE for **testosterone** was higher than that of excised hairless-rat skin. The metabolism of ester prodrugs of TS in LSE was dependent on their physicochem. properties and susceptibility to enzymic hydrolysis. Application of acetyl-TS and benzoyl-TS resulted in a high formation of the 17-dehydrogenated metabolite, androstenedione (ADO), though a very small amount of the **prodrug** was observed in the dermal side. Succinoyl-TS, a hydrophilic ester with very low susceptibility to hydrolysis, was quite resistant to both 5α-reduction and 17-dehydrogenation, and more than 90% of the radioactivity appearing on the dermal side was from the **prodrug** itself and from TS. The hydrophilic and enzymically stable TS derivative may be a good candidate compound with which to administer TS transdermally.

L2 ANSWER 30 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:181570 HCAPLUS
DOCUMENT NUMBER: 124:233011
TITLE: Preparation of glycoside prodrugs with enhanced water solubility.
INVENTOR(S): Klemke, R.-Erich; Koreeda, Masato; Houston, Todd A.; Shull, Brian K.; Tuinman, Roeland J.
PATENT ASSIGNEE(S): Harrier, Inc., USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9532981	A1	19951207	WO 1995-US7027	19950601
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5693767	A	19971202	US 1994-251869	19940601
AU 9526617	A1	19951221	AU 1995-26617	19950601
PRIORITY APPLN. INFO.:			US 1994-251869 A	19940601
			US 1991-644002 A2	19910122
			US 1991-733915 B2	19910722
			US 1992-815691 B2	19920124

US 1993-6447 B2 19930121
WO 1995-US7027 W 19950601

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Glycosides of aliphatic, alicyclic, aliphatic-aromatic, and aromatic aglycons having primary, secondary, or tertiary OH, SH, or CO2H groups with 2,3-dideoxy-α-D-erythrohex-2-enopyranoside fragments Q1-Q6 (A = acyl; X = O, S, CO2), were prepared Thus, a mixture of 4-acetamidophenol and hexaacetyl D-maltal was refluxed with iodine in THF for 12 h to give 30% of an α,β-glycoside, which was stirred with Ba(OH)2 in MeOH to give glycoside (I). I had 8 times the H2O solubility of tylenol itself in phosphate-buffered saline at pH 7.4.

L2 ANSWER 31 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:135052 HCAPLUS
DOCUMENT NUMBER: 124:249920
TITLE: Synthesis of novel androgen-linked phosphoramide mustard prodrugs and growth-inhibitory activity in human breast cancer cells
AUTHOR(S): Roth, T.; Tang, W.; Eisenbrand, G.
CORPORATE SOURCE: Dep. Chem., Univ. Kaiserslautern, Kaiserslautern, D-67663, Germany
SOURCE: Anti-Cancer Drug Design (1995), 10(8), 655-66
CODEN: ACDDEA; ISSN: 0266-9536
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two androgen-linked phosphoramide mustard prodrugs were synthesized. The androgens **testosterone** and 19-nortestosterone were linked through the 17β-position via an acetal bond to aldophosphamide. Proton-catalyzed, as well as cytochrome P 450-mediated cleavage of the acetal bond resulted in the release of aldophosphamide which decays into the ultimate cytotoxic species, phosphoramide mustard. In a competitive cellular binding assay, the new prodrugs displayed .apprx.10-12% affinity to androgen binding proteins in breast cancer cells, relative to **testosterone** (100%). In the sex hormone receptor-neg. cell line MDA-MB231, the **testosterone** and 19-nortestosterone conjugates have been found to be as effective as 4-hydroperoxycyclophosphamide. Both compds. were more active than 4-hydroperoxycyclophosphamide in receptor-pos. cell lines. No significant differences in response were observed, however, between receptor-neg. and receptor-pos. cell lines.

L2 ANSWER 32 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:784119 HCAPLUS
DOCUMENT NUMBER: 123:161032
TITLE: **Prodrug** versus drug effects of 150 μg desogestrel or 3-keto-desogestrel combination with 30 μg ethinylestradiol on hormonal parameters: relevance of the peak serum level of 3-keto-desogestrel
AUTHOR(S): Kuhl, H.; Jing-Hoffmann, C.; Fitzner, M.
CORPORATE SOURCE: Dep. Obstetrics Gynecology, J. W. Goethe Univ., Frankfurt-am-Main, Germany

09872705

SOURCE: Hormone Research (1995), 44(3), 126-32
CODEN: HRMRA3; ISSN: 0301-0163
PUBLISHER: Karger
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The pharmacokinetics and pharmacodynamics of 150 μg desogestrel (DG) or 150 μg 3-keto-desogestrel (KDG) in combination with 30 μg ethinylestradiol (EE) were compared in a cross-over study. While the EE levels as well as the area under the curve (AUC) of KDG did not differ, significantly higher peak levels of KDG were observed after intake of the KDG-containing formulation. As compared to the control cycle, LH and FSH were not reduced on day 3 of the first treatment cycle (3/I), but markedly suppressed on day 21 of the third cycle (21/III), the effects being more pronounced with the DG-containing pill. The serum levels of **testosterone**, free **testosterone**, androstenedione, androstanediol glucuronide, and dehydroepiandrosterone sulfate (DHEA-S) were significantly reduced already on day 3/I, while sex hormone-binding globulin (SHBG) was unchanged and corticosteroid-binding globulin (CBG) was increased. Thereafter, both SHBG and CBG rose markedly. The progressive decrease in DHEA-S correlated best with free **testosterone** and androstanediol glucuronide. The results indicate that the peak level of KDG is more important for the biol. effectiveness than the AUC or KDG which appears to antagonize the suppressive action of EE on gonadotropin release. The rapid decrease in the androgen levels seems to be due to a direct inhibitory action of the pill on ovarian and adrenal steroid biosynthesis.

L2 ANSWER 33 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:342893 HCAPLUS
DOCUMENT NUMBER: 122:142214
TITLE: Transdermal delivery of **testosterone** using micellar **prodrug** approach
AUTHOR(S): Thassu, Deepak; Singh, M.; Vyas, S. P.
CORPORATE SOURCE: RANBAXY LABORATORIES LIMITED, New Delhi, 110020, India
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1994), 21ST, 463-4
CODEN: PCRMEY; ISSN: 1022-0178
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Amelioration of lipophilicity of **testosterone** by incorporating hydrophilic nontoxic bioacceptable chemical moieties and thus achieving optimum structural configuration to get enhanced transdermal permeation across the viable skin was investigated. The benefit of this micellar **prodrug** approach was the production of non-cytotoxic metabolites, protection of drug from cutaneous metabolism, and thus improved bioavailability and concomitant reduction in side effects.

L2 ANSWER 34 OF 48 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:229213 HCAPLUS
DOCUMENT NUMBER: 122:10363
TITLE: Preparation of **prodrug** esters
INVENTOR(S): Budt, Karl-Heinz; Peyman, Anuschirwan
PATENT ASSIGNEE(S): Hoechst A.-G., Germany
SOURCE: Ger. Offen., 29 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4308095	A1	19940915	DE 1993-4308095	19930313
PRIORITY APPLN. INFO.:			DE 1993-4308095	19930313

OTHER SOURCE(S): MARPAT 122:10363

AB W(R5)a [I; R5 = e.g., O2C(CR11R12)sX(CR15R16)lNR21[(CR15R16)mNR21]oR24; R11,R12,R15,R16 = H or alkyl; R21 = H, (cyclo)alkyl, alkoxycarbonyl; R24 = H, (cyclo)alkyl, alkenyl, aryl, etc.; W = mono-, di-, or tri-dehydroxylated drug residue; X = O, S, (alkyl)imino, etc.; a = 1-3; l = 2 or 3; o = 0-3; s = 1-5] were prepared Thus, **testosterone** was bromoacetylated and the product condensed with MeNHCH2CH2NMeCO2CMe3 (preparation given) to give, after deprotection, I (R5 = O2CCH2NMeCH2CH2NHMe, W = dehydroxylated **testosterone** residue, a= 1).

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Searching 1976 to present...

Results of Search in 1976 to present db for:
(androgen AND prodrugs): 245 patents.
*Hits **1** through **50** out of **245***

Next 50 Hits

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Refine Search androgen and prodrugs

	PAT. NO.	Title
1	6,884,795	Pharmaceutical compositions and uses for androst-5-ene-3.beta., 17.beta.-diol
2	6,881,728	14-.beta., 17-.alpha.-hydroxymethylandrostane derivatives as androgens
3	6,878,806	Human secreted protein HTEEB42
4	6,875,886	Modified PSMA ligands and uses related thereto
5	6,875,767	(5-cyano-2-thiazolyl)amino-4-pyridine tyrosine kinase inhibitors
6	6,872,724	Polymorphs with tyrosine kinase activity
7	6,872,715	Benzoquinone ansamycins
8	6,864,275	Compounds and methods for use thereof in the treatment of cancer
9	6,858,627	Glucocorticoid mimetics, methods of making them, pharmaceutical compositions, and uses thereof
10	6,858,598	Method of using a matrix metalloproteinase inhibitor and one or more antineoplastic agents as a combination therapy in the treatment of neoplasia
11	6,855,836	17-Methylene steroids, process for their production and pharmaceutical compositions that contain these compounds
12	6,852,719	Glucocorticoid receptor modulators
13	6,852,709	Biologically useful polyphosphates
14	6,849,649	N-phenpropylcyclopentyl-substituted glutaramide derivatives as inhibitors of neutral endopeptidase
15	6,846,839	Methods for treating diseases and disorders related to unregulated angiogenesis and/or vasculogenesis
16	6,846,823	Method of treating lower urinary tract disorders
17	6,846,809	PEI: DNA vector formulations for in vitro and in vivo gene delivery

18 6,838,584 T Estrogen receptor modulators
19 6,835,392 T Dual enhancer composition for topical and transdermal drug delivery
20 6,833,373 T Method of using an integrin antagonist and one or more antineoplastic agents as a combination therapy in the treatment of neoplasia
21 6,833,372 T Non-peptide GnRH agents, Pharmaceutical compositions, and methods for their use
22 6,831,102 T Phenyl naphthol ligands for thyroid hormone receptor
23 6,824,993 T Antibodies that bind human prostate specific G-protein receptor HPRAJ70
24 6,824,780 T Anti-tumor antibody compositions and methods of use
25 6,818,226 T Dermal penetration enhancers and drug delivery systems involving same
26 6,812,344 T 1-(4-Arylpiperazin-1-yl)-.omega.-[N-(.alpha.,.omega.-dicarboximidoL)]-alkan es useful as uro-selective .alpha.1-adrenoceptor blockers
27 6,809,193 T Antisense oligonucleotide compositions and methods for the modulation of JNK proteins
28 6,805,876 T Phosphate based biodegradable polymers
29 6,800,655 T Analogs of indole-3-carbinol metabolites as chemotherapeutic and chemopreventive agents
30 6,797,704 T Systemic delivery of compounds through non-invasive bladder administration
31 6,794,393 T Tyrosine kinase inhibitors
32 6,794,363 T Isolated amyloid inhibitor protein (APIP) and compositions thereof
33 6,784,170 T Synthesis of anti-estrogenic and other therapeutic steroids from 21-hydroxy-19-norpregna-4-en-3-one
34 6,784,167 T 17-beta-hydroxysteroid dehydrogenase-II inhibitors
35 6,780,854 T Orally active androgens
36 6,770,466 T Human protein tyrosine phosphatase polynucleotides, polypeptides, and antibodies
37 6,759,431 T Compositions and methods for treating or preventing diseases of body passageways
38 6,756,397 T Prodrugs of CC-1065 analogs
39 6,753,164 T Nucleic acids encoding human serpin polypeptide HMCIS41
40 6,750,213 T Estrogen receptor modulators
41 6,750,019 T Antisense modulation of insulin-like growth factor binding protein 5 expression
42 6,747,048 T Pyridine-based thyroid receptor ligands
43 6,740,646 T Bioavailable prodrugs of androgenic steroids and related method
44 6,740,333 T Suppository and composition comprising at least one polyethylene glycol
45 6,734,211 T Compositions and methods for promoting nerve regeneration
46 6,734,185 T Pyrrolo[3,4-d]pyrimidines as corticotropin releasing factor (CRF) antagonists
47 6,723,730 T Capsaicin receptor ligands
48 6,720,344 T Methods and compositions for stimulating osteoblast proliferation or treating malignant cell proliferation and methods for selecting osteoblast proliferation stimulants
49 6,716,821 T Cytotoxic agents bearing a reactive polyethylene glycol moiety, cytotoxic conjugates comprising polyethylene glycol linking groups, and methods of making and using the same
50 6,713,487 T Compounds useful as modulators of melanocortin receptors and pharmaceutical compositions comprising same

USPTO Patent Full-Text and Image Database

Searching 1976 to present...

Results of Search in 1976 to present db for:
((testosterone AND prodrugs) AND ether): 426 patents.
Hits 1 through 50 out of 426

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Refine Search testosterone and prodrugs and ether

	PAT. NO.	Title
1	6,884,795	Pharmaceutical compositions and uses for androst-5-ene-3.beta., 17.beta.-diol
2	6,884,787	Antisense modulation of transforming growth factor-beta 3 expression
3	6,881,728	14-.beta., 17-.alpha.-hydroxymethylandrostane derivatives as androgens
4	6,878,806	Human secreted protein HTEEB42
5	6,878,805	Peptide-conjugated oligomeric compounds
6	6,878,709	3,4-di-substituted pyridazinediones as CXC chemokine receptor antagonists
7	6,878,697	Phenylamino-pyrimidines and uses thereof
8	6,875,886	Modified PSMA ligands and uses related thereto
9	6,870,046	Antisense modulation of interferon gamma receptor 2 expression
10	6,869,952	Pyrrolo[2,1-f][1,2,4]triazine inhibitors of kinases
11	6,867,039	Antisense modulation of dual specific phosphatase 5 expression
12	6,864,275	Compounds and methods for use thereof in the treatment of cancer
13	6,861,418	4-aryl substituted indolinones
14	6,858,627	Glucocorticoid mimetics, methods of making them, pharmaceutical compositions, and uses thereof
15	6,855,730	3-methylidenyl-2-indolinone modulators of protein kinase
16	6,855,700	Antisense modulation of damage-specific DNA binding protein 1, p127 expression
17	6,852,536	Antisense modulation of CD36L 1 expression
18	6,849,649	N-phenpropylcyclopentyl-substituted glutaramide derivatives as inhibitors of neutral endopeptidase
19	6,846,925	Colchinol derivatives as angiogenesis inhibitors

20 6,846,809 T PEI: DNA vector formulations for in vitro and in vivo gene delivery
21 6,844,010 T Therapeutic treatment and prevention of infections with a bioactive materials encapsulated within a biodegradable-biocompatible polymeric matrix
22 6,838,283 T Antisense modulation of survivin expression
23 6,835,392 T Dual enhancer composition for topical and transdermal drug delivery
24 6,833,372 T Non-peptide GnRH agents, Pharmaceutical compositions, and methods for their use
25 6,828,151 T Antisense modulation of hematopoietic cell protein tyrosine kinase expression
26 6,828,149 T Antisense modulation of PPP3R1 expression
27 6,825,337 T Antisense modulation of PLML expression
28 6,825,201 T Indole, azaindole and related heterocyclic amidopiperazine derivatives
29 6,825,198 T 5-HT receptor ligands and uses thereof
30 6,821,978 T Xanthine phosphodiesterase V inhibitors
31 6,818,668 T 5-alkyl-7-alkylcarbonate-isoflavone ester and related method
32 6,818,226 T Dermal penetration enhancers and drug delivery systems involving same
33 6,818,213 T Cancer treatment compositions comprising therapeutic conjugates that bind to aminophospholipids
34 6,809,193 T Antisense oligonucleotide compositions and methods for the modulation of JNK proteins
35 6,800,751 T Reagent and process for protecting nucleoside hydroxyl groups
36 6,797,819 T Alkaloids
37 6,797,725 T Prodrugs of a 3-(pyrrol-2-ylmethylidene)-2-indolinone derivatives
38 6,794,406 T Indole derivatives
39 6,794,363 T Isolated amyloid inhibitor protein (APIP) and compositions thereof
40 6,793,938 T Biodegradable compositions for the controlled release of encapsulated substances
41 6,784,170 T Synthesis of anti-estrogenic and other therapeutic steroids from 21-hydroxy-19-norpregna-4-en-3-one
42 6,784,167 T 17-beta-hydroxysteroid dehydrogenase-II inhibitors
43 6,783,760 T Combined cancer treatment methods using therapeutic conjugates that bind to aminophospholipids
44 6,780,854 T Orally active androgens
45 6,780,853 T Neuroactive steroids of the androstane and pregnane series
46 6,777,417 T 3-(4,5,6,7-tetrahydroindol-2-ylmethylidiene-2-indolinone derivatives as kinase inhibitors
47 6,770,466 T Human protein tyrosine phosphatase polynucleotides, polypeptides, and antibodies
48 6,767,739 T Antisense modulation of microsomal triglyceride transfer protein expression
49 6,763,607 T Method for making homogeneous spray-dried solid amorphous drug dispersions utilizing modified spray-drying apparatus
50 6,762,025 T Single-molecule selection methods and compositions therefrom

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USPTO PATENT FULL-TEXT AND IMAGE DATABASE

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Results of Search in 1976 to present db for:
(testosterone AND ((prodrug AND ether) AND androgen)): 128 patents.
*Hits **1** through **50** out of **128***

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Refine Search testosterone and (prodrug and ether and androgen le

	PAT. NO.	Title
1	6,884,795	Pharmaceutical compositions and uses for androst-5-ene-3.beta., 17.beta.-diol
2	6,878,806	Human secreted protein HTEEB42
3	6,875,886	Modified PSMA ligands and uses related thereto
4	6,864,275	Compounds and methods for use thereof in the treatment of cancer
5	6,858,627	Glucocorticoid mimetics, methods of making them, pharmaceutical compositions, and uses thereof
6	6,858,621	2-(quinolonyl)-fused heterocycles as androgen receptor modulators
7	6,849,649	N-phenpropylcyclopentyl-substituted glutaramide derivatives as inhibitors of neutral endopeptidase
8	6,846,809	PEI: DNA vector formulations for in vitro and in vivo gene delivery
9	6,835,392	Dual enhancer composition for topical and transdermal drug delivery
10	6,833,372	Non-peptide GnRH agents, Pharmaceutical compositions, and methods for their use
11	6,831,093	Non-steroidal ligands for the glucocorticoid receptor, compositions and uses thereof
12	6,818,226	Dermal penetration enhancers and drug delivery systems involving same
13	6,809,193	Antisense oligonucleotide compositions and methods for the modulation of JNK proteins
14	6,794,363	Isolated amyloid inhibitor protein (APIP) and compositions thereof
15	6,787,531	Pharmaceutical composition for use as a contraceptive
16	6,784,167	17-beta-hydroxysteroid dehydrogenase-II inhibitors
17	6,770,466	Human protein tyrosine phosphatase polynucleotides, polypeptides, and antibodies
18	6,753,164	Nucleic acids encoding human serpin polypeptide HMCIS41

19 6,750,019 T Antisense modulation of insulin-like growth factor binding protein 5 expression
20 6,747,048 T Pyridine-based thyroid receptor ligands
21 6,735,470 T Electrokinetic delivery of medicaments
22 6,713,487 T Compounds useful as modulators of melanocortin receptors and pharmaceutical compositions comprising same
23 6,710,086 T Protected forms of pharmacologically active agents and uses therefor
24 6,706,700 T 14.beta.,15.beta.-methylene-17.alpha.-hydroxymethyl-androgens
25 6,696,484 T Method and compositions for regulation of 5-alpha reductase activity
26 6,670,386 T Bicyclic modulators of androgen receptor function
27 6,670,346 T Medical uses of a selective estrogen receptor modulator in combination with sex steroid precursors
28 6,660,760 T Heterocyclic aromatic compounds useful as growth hormone secretagogues
29 6,660,756 T N-phenpropylcyclopentyl-substituted glutaramide derivatives as inhibitors of neutral endopeptidase
30 6,649,587 T Polyamine analog conjugates and quinone conjugates as therapies for cancers and prostate diseases
31 6,632,834 T Compositions and methods for treating conditions responsive to estrogen
32 6,630,453 T Androgen derivatives and uses thereof
33 6,607,916 T Antisense inhibition of Casein kinase 2-alpha expression
34 6,605,441 T Antibodies against fibroblast growth factor 11
35 6,602,902 T Dha-pharmaceutical agent conjugates to improve tissue selectivity
36 6,593,112 T Polynucleotides encoding fibroblast growth factor 15
37 6,586,000 T Hydroxide-releasing agents as skin permeation enhancers
38 6,583,179 T Substituted aminoalkylamide derivatives as antagonists of follicle stimulating hormone
39 6,582,724 T Dual enhancer composition for topical and transdermal drug delivery
40 6,576,636 T Method of treating a liver disorder with fatty acid-antiviral agent conjugates
41 6,573,289 T Naphthalene derivatives, their production and use
42 6,562,370 T Transdermal administration of steroid drugs using hydroxide-releasing agents as permeation enhancers
43 6,525,203 T Heterocyclic aromatic compounds useful as growth hormone secretagogues
44 6,518,292 T Heterocyclic aromatic compounds usefuls as growth hormone secretagogues
45 6,518,257 T 1-substituted phenyl-1-(1h-imidazol-4-yl) alcohols, process for producing the same and use thereof
46 6,512,002 T Methods of treatment for premature ejaculation in a male
47 6,477,410 T Electrokinetic delivery of medicaments
48 6,465,445 T Medical uses of a selective estrogen receptor modulator in combination with sex steroid precursors
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50 6,440,738 T Antisense modulation of casein kinase 2-beta expression

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	PAT. NO.	Title
1	6,885,895	Methods and systems for electrical and/or drug stimulation as a therapy for erectile dysfunction
2	6,884,842	Molecular compounds having complementary surfaces to targets
3	6,884,795	Pharmaceutical compositions and uses for androst-5-ene-3.beta., 17.beta.-diol
4	6,884,787	Antisense modulation of transforming growth factor-beta 3 expression
5	6,884,601	Method to detect fertilization potential of sperm
6	6,884,418	Use of ligand-mimicking agents and anti-neoplastic drugs in cancer therapy
7	6,882,940	Methods and devices for prediction of hypoglycemic events
8	6,881,789	Polyubiquitin based hydrogel and uses thereof
9	6,881,729	Bile compound and method of controlling behavior of lampreys therewith
10	6,881,728	14-.beta., 17-.alpha.-hydroxymethylandrostane derivatives as androgens
11	6,881,548	Methods and kits for diagnosing tumorigenicity and determining resistance to the antineoplastic effects of antiestrogen therapy
12	6,881,423	Powdery composition for nasal administration
13	6,881,421	Nanoparticles comprising at least one polymer and at least one compound able to complex one or more active ingredients
14	6,878,806	Human secreted protein HTEEB42
15	6,878,805	Peptide-conjugated oligomeric compounds
16	6,878,731	Imidazole alkaloids from Lepidium meyenii and methods of usage
17	6,878,709	3,4-di-substituted pyridazinediones as CXC chemokine receptor antagonists
18	6,878,697	Phenylamino-pyrimidines and uses thereof

19 6,878,548 Composition for use in electroporation
20 6,878,547 Antisense oligonucleotides against tenascin for treating vitiligo
21 6,878,529 Compounds for the treatment of sexual dysfunction
22 6,875,886 Modified PSMA ligands and uses related thereto
23 6,875,854 Compositions and methods for the improved diagnosis and treatment of germ cell tumors
24 6,875,843 Prevention of diabetes and prolongation of the honeymoon phase of diabetes by administration of GnRH antagonists
25 6,875,619 Microfluidic devices comprising biochannels
26 6,875,606 Human .alpha.-7 nicotinic receptor promoter
27 6,875,597 Isolated human drug-metabolizing proteins, nucleic acid molecules encoding human drug-metabolizing proteins, and uses thereof
28 6,875,438 Preparations for topical administration of substances having antiandrogenic activity
29 6,875,180 Electromagnetic interference immune tissue invasive system
30 6,872,811 HRPCa9 and HRPCa10 nucleic acids and polypeptides
31 6,872,569 In vitro production of haploid germ cells
32 6,872,546 Hyaluronan-binding proteins and encoding genes
33 6,872,406 Fusogenic properties of saposin C and related proteins and polypeptides for application to transmembrane drug delivery systems
34 6,870,046 Antisense modulation of interferon gamma receptor 2 expression
35 6,869,973 Nitrosated and nitrosylated taxanes, compositions and methods of use
36 6,869,952 Pyrrolo[2,1-f][1,2,4]triazine inhibitors of kinases
37 6,867,216 Inhibitors of hedgehog signal pathways, compositions and uses related thereto
38 6,867,039 Antisense modulation of dual specific phosphatase 5 expression
39 6,867,005 Method and apparatus for increasing the dynamic range and accuracy of binding assays
40 6,864,275 Compounds and methods for use thereof in the treatment of cancer
41 6,864,250 N-acylated lipophilic amino acid derivatives
42 6,864,248 Androgenic steroid compounds and a method of making and using the same
43 6,864,245 Biocompatible poly-.beta.-1.fwdarw.4-N-acetylglucosamine
44 6,864,103 Phthalamide-lanthanide complexes for use as luminescent markers
45 6,863,902 Immediate release eplerenone compositions
46 6,862,890 Process for production of nanoparticles and microparticles by spray freezing into liquid
47 6,862,479 Spinal cord stimulation as a therapy for sexual dysfunction
48 6,861,557 Process for preparing rac-bicalutamide and its intermediates
49 6,861,508 Transcriptional intermediary factor-2
50 6,861,432 Piperazine derivatives that destabilize androgen receptors

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